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A New History and Discussion of 180-Day Exclusivity

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Congress created 180-day exclusivity for generic drug applicants in the 1984 Hatch-Waxman amendments to the Federal Food, Drug, and Cosmetic Act (FDCA)[1] and amended the provision substantially in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA).[2] The fundamental goal behind 180-day exclusivity was to provide an incentive for generic drug applicants to challenge innovator patents, and the core of the concept—as it has been applied by the Food and Drug Administration (FDA) and the courts—is that the first generic drug applicant to challenge an innovator's patent is entitled to six months of exclusivity against subsequent patent challengers for the same innovator drug. 180-day exclusivity is governed by sections 505(j)(5)(B)(iv) and 505(j)(5)(D) of the FDCA.

Although the basic idea is simple and the language enacted in 1984 was correspondingly brief, over the years the provision gave rise to a substantial number of interpretive disputes both at the agency and in the courts. More than five years have passed since enactment of the 2003 revisions, and the law governing the 1984 provisions is nearly settled.[3] Applicants and the agency have begun to grapple with interpretation of the new provisions enacted in 2003, and although the new provisions appear likely to raise interpretive issues that will be vigorously contested, to date there have been no court decisions.

This is the third in a series of articles on 180-day exclusivity. The first article traced the history of 180-day exclusivity from 1984 through its amendment in 2003 and court cases in 2004.[4] A second article, published by two of the authors in 2007, updated the earlier piece through the end of 2006 but was arranged by issue rather than in a chronology.[5] This article, which includes a third author, provides

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[1] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

[2] Pub. L. No. 108-173, 117 Stat. 2066 (2003).

[3] There is one citizen petition pending relating to the old rules. *See* Apotex, Inc., Petition for Stay of Action, Docket No. FDA-2008-P-0117 (Feb. 13, 2008) (pending); It, however, should be considered moot in light of a recent court decision upholding the validity of the patent at issue. At a Food and Drug Law Institute (FDLI) conference on the Hatch-Waxman Amendments (Feb. 5, 2009), Elizabeth Dickinson—Associate Chief Counsel for Drugs, Office of the Chief Counsel, FDA—stated that there are roughly 12 innovator products with ANDAs pending that are subject to the old rules.

[4] Erika Lietzan, *A Brief History of 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, 59 FOOD & DRUG L.J. 287 (2004). A subsequent update traced developments in 2004. Erika Lietzan, *2004 Update—180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, 59 FOOD & DRUG L.J. 459 (2004).

[5] Erika Lietzan, & David E. Korn, *Issues in the Interpretation of 180-Day Exclusivity*, 62 FOOD & DRUG L. J. 49 (2007).

a comprehensive resource on 180-day exclusivity for old abbreviated new drug applications (ANDAs)[6] (but less detail in some places where the 2007 article may be referenced) but focus more discussion on the new provisions as well as some policy and legal issues related to 180-day exclusivity that the authors have not previously addressed.

I. BACKGROUND

A. *Original Statutory Language*

Between 1984 and 2003, section 505(j)(5)(B)(iv) of the FDCA provided that:

> [i]f the [abbreviated new drug] application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) [otherwise known as a "paragraph IV certification"[7]] and is for a drug for which a previous application has been submitted under this subsection continuing [*sic* "containing"] such a certification, the application shall be made effective not earlier than one hundred and eighty days after—(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.[8]

Put another way, the first[9] generic applicant to file an ANDA containing a paragraph IV certification was to be awarded 180 days of exclusivity, during which FDA could not approve a subsequent ANDA that challenged a patent for the same drug product. The 180 days was calculated from either the date of the first commercial marketing of the generic drug product by the first applicant (with a paragraph IV certification) or the date of a court decision declaring the patent invalid or not infringed, whichever was earlier.

B. *Revised Statutory Language*

Section 505(j)(5)(B)(iv) now provides that:

> [i]f the [abbreviated new drug] application contains a certification described in paragraph (2)(A)(vii)(IV) [a paragraph IV certification] and is a drug for which a first applicant has submitted an application containing such a

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[6] The authors refer to ANDAs subject to the original provisions as "old ANDAs" and ANDAs subject to the 2003 legislation as "new ANDAs."

[7] A company seeking approval of a generic product must submit with its ANDA a certification with respect to each patent that claims the reference drug or claims a use of the reference drug. 21 U.S.C. § 355(j)(2)(A)(vii). If the ANDA applicant seeks to market its product prior to expiration of any such patent, the ANDA applicant submits a "paragraph IV certification" asserting that the patent for which the certification is submitted is invalid or will not be infringed by the proposed generic product. 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

[8] 21 U.S.C. § 355(j)(5)(B)(iv) (1984) (amended 2003).

[9] Although the statute referred to "previous" ANDAs, it was interpreted over time to mean that only the first applicant was eligible. *See, e.g.*, 64 Fed. Reg. 42,873, 42,875 (Aug. 6, 1999) (stating that FDA's regulations "interpret[] the statute as allowing eligibility for exclusivity only for the applicant that submits the first substantially complete ANDA with a paragraph IV certification").

> certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.[10]

In short, as before, the first generic applicant to file an ANDA containing a paragraph IV certification is awarded 180 days of marketing exclusivity, during which FDA may not approve a subsequently filed ANDA that challenged a patent for the same drug product. The exclusivity period is now calculated from the date of the first commercial marketing of the drug product (including the listed drug product) by a first applicant. A court decision does not start the exclusivity period for new ANDAs.

Congress also added an elaborate provision governing forfeiture of 180-day exclusivity. Under section 505(j)(5)(D), the 180-day exclusivity period is forfeited by a first applicant if the applicant fails to market the drug by the later of: 1) 75 days after the date on which approval of its application is effective, or 30 months after its application was submitted, whichever is earlier; or 2) 75 days after the date on which, as to each patent that is the subject of a paragraph IV certification by the first applicant (qualifying it for exclusivity), a court finds the patent invalid or not infringed, a court signs a settlement order or consent decree finding the patent invalid or not infringed, or the patent information is withdrawn by the holder of the approved new drug application (NDA). The first applicant also forfeits the exclusivity period if any of the following occurs: 1) the first applicant withdraws its application or FDA considers it withdrawn because it did not meet the requirements for approval; 2) the first applicant amends or withdraws all of the paragraph IV certifications that qualified it for exclusivity; 3) the first applicant fails to obtain tentative approval of its application within 30 months after it was filed (unless the failure is caused by a change in or review of the requirements for approval of the application imposed after it was filed); 4) the first applicant enters into an agreement with another ANDA applicant, the NDA holder, or a patent holder, and the Federal Trade Commission (FTC) or a court finds that the agreement violates the antitrust laws; or 5) all of the patents as to which the first applicant filed a paragraph IV certification qualifying it for exclusivity have expired. Forfeiture events are determined individually for each first applicant. If all first applicants forfeit their 180-day exclusivity, any subsequent ANDA approval may be made effective immediately; exclusivity does not roll over to a subsequent ANDA applicant.[11]

Congress also added definitions to the statute for "180-day exclusivity period," "first applicant," "substantially complete application," and "tentative approval." Some of these reflected new concepts. A "first applicant" is "an applicant that, on the first day on which a substantially complete application containing a [paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug."[12] A "substantially complete application" means "an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by [section 505(j)(2)(A)]."[13]

In general, the amended provisions apply only to ANDAs filed after December 8, 2003, and only if there was no paragraph IV certification to the listed drug prior

[10] 21 U.S.C. § 355(j)(5)(B)(iv)(I) (2003).
[11] 21 U.S.C. § 355(j)(5)(D).
[12] 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb).
[13] 21 U.S.C. § 355(j)(5)(B)(iv)(II)(cc).

to that date.[14] The exceptions relate to the "court decision" trigger for exclusivity, described below in section II.B.3.a., and the forfeiture event for certain settlement agreements, discussed below in section III.A.6.

C. *FDA's Approach to Interpreting the Exclusivity Provisions*

The 2003 amendments to the 180-day exclusivity provisions have created two paradigms governing 180-day exclusivity (three, if one counts the paradigm before the 2003 changes that were retroactive). The agency's interpretation of the old statutory provisions was fleshed out in regulations, guidance, and responses to citizen petitions, and—as discussed below—the federal courts played a significant role in shaping this interpretation. The agency has proposed no regulations to implement the new statutory provisions, it has issued only one draft guidance,[15] and no court has interpreted the new provisions. Moreover, at the end of February 2009, only three petitions relating to 180-day exclusivity submitted since the authors' last article were pending before FDA,[16] and there were no open dockets requesting comments on an exclusivity issue.

The dearth of pending petitions and open dockets before FDA may be due, in part, to the fact that the agency and courts resolved many of the interpretative issues concerning the pre-2003 statutory language and the fact that many of the rules and policies governing 180-day exclusivity for new ANDAs are presumed to be the same. Another explanation may be that the agency has been addressing new interpretative issues more quickly than it did the older issues.

Between 2007 and 2008, FDA received approximately 13 petitions relating to 180-day exclusivity issues,[17] and it opened five nonrulemaking dockets. The agency responded to nine of these petitions in approximately seven months or fewer. Three petitions are currently pending, and one was withdrawn. FDA also issued its responses in the five nonrulemaking dockets within eight months. During the previous

[14] *See* Pub. L. No. 108-173 § 1102(b)(1), 117 Stat. 2066, 2460 (2003); FDA, Draft Guidance for Industry, Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Questions and Answers 12 (Oct. 2004). FDA recently announced that when one or more ANDAs were submitted to the agency before December 8, 2003, but the first paragraph IV certification was submitted after December 3, 2003, it would apply the pre-MMA statutory 180-day exclusivity provisions to these applications. Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to ANDA Applicants (Apr. 15, 2009).

[15] *See* FDA, Draft Guidance for Industry, Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Questions and Answers (Oct. 2004).

[16] *See* Novo Nordisk, Inc., Petition for Reconsideration, Docket No. FDA-2008-P-0343 (Dec. 19, 2008); Novo Nordisk Inc., Petition for Stay of Action, Docket No. FDA-2008-P-0343 (Dec. 20, 2008); Apotex, Inc., Petition for Stay of Action, Docket No. FDA-2008-P-0117 (Feb. 13, 2008). Of the three outstanding petitions, two were submitted in December 2008 in response to a denial by FDA of the filer's initial petition. Although FDA has not responded to the other remaining petition, that petition should be considered moot due to a recent court decision upholding the validity of the patent at issue.

[17] The authors count separately any filing styled as a petition—for example, a citizen petition, a petition for stay of action, or a petition for reconsideration—if it related to 180-day exclusivity. Separate petitions were counted separately, even if filed by the same party relating to the same product. The authors have included two petitions submitted by Cobalt concerning bioequivalence issues because they were relevant to FDA's determination that Cobalt did not forfeit its period of 180-day exclusivity due to a failure to obtain tentative approval in a timely fashion. The authors have also included four petitions submitted by Novo Nordisk and Caraco regarding whether Caraco may submit, with its ANDA to market a generic version of Prandin (repaglinide), a split certification—meaning both a paragraph IV certification and a section viii statement—with respect to Novo Nordisk's patent, which includes separate claims for the drug and a method of using the drug. A "section viii statement," authorized by section 505(j)(2)(A)(viii) of the FDCA, refers to a method of use patent listed in the *Orange Book* which does not claim a use for which the applicant seeks approval. 21 U.S.C. § 355(j)(2)(A)(viii). FDA's decision in this matter affects whether Caraco, as the first applicant to submit an ANDA to market generic repaglinide, will be able to retain its split certification and thus whether it will be eligible for 180-day exclusivity based on its paragraph IV certification.

two-year period, between 2005 and 2006, FDA received about half as many petitions and opened no dockets relating to 180-day exclusivity. While it responded to two related petitions within one month of receiving them, it took the agency an average of approximately 10 months to respond to the other three petitions it received. One of the six petitions received during 2005 and 2006 was withdrawn.

The increased pace of FDA's responses to more recent interpretative issues may be explained in part by the fact that when the agency opens a nonrulemaking docket, the issue to be addressed is typically one with an impending deadline (e.g., final approval of an ANDA or ANDAs and an exclusivity determination). In addition, seven of the 13 petitions submitted between 2007 and 2008 included a certification under new section 505(q) of the FDCA, which requires FDA to respond to certain petitions requesting action on pending ANDAs within 180 days.[18]

Just under half of the petitions submitted in 2007 and 2008 concerned agency practice with respect to the application of the old statutory provisions. This percentage will decrease in the future, because—as noted above—there are few products for which old ANDAs are currently pending.[19] Of the five nonrulemaking dockets the agency opened over the last two years to address 180-day exclusivity issues, one concerned the application of the old provisions, three concerned the application of the new provisions (specifically the forfeiture provisions), and one concerned the application of both the new and old provisions (including the settlement agreement forfeiture provision). At least four of these five dockets appear to have been initiated in response to a letter or a lawsuit seeking particular action with respect to an ANDA or ANDAs. The agency has used these dockets to address complex interpretative issues, particularly in the case of the forfeiture provisions, by seeking input from interested parties.[20] While this practice is not new,[21] the frequency with which FDA has opened nonrulemaking dockets related to 180-day exclusivity issues in the last two years appears to be without precedent.

Some observers have criticized the agency's use of nonrulemaking dockets, in lieu of rulemaking, to address issues related to forfeiture. They have expressed concern that this practice "reduces the certainty" for ANDA applicants and thus "limits their ability to plan" due to the lack of guidance from the agency.[22] Some also contend that FDA's practice of making decisions on a case-by-case basis instead of considering forfeiture issues more broadly in a rulemaking may weaken the agency's position in lawsuits.[23] In light of this practice and the concerns associated with it, some have speculated that the courts will play a significant role in interpreting the

[18] *See* 21 U.S.C. § 355(q)(1)(F). Section 505(q) does not, however, apply to "a petition that relates solely to the timing of the approval of an application pursuant to [the 180-day exclusivity provision]." 21 U.S.C. § 355(q)(4)(A).

[19] *See supra* text accompanying note 3.

[20] The agency has stated that it established these dockets in recognition of the "substantial interest" in forfeiture events and to obtain comments from interested parties on the interpretation and application of the provisions. FDA, Decision Letter: Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008), at 5; FDA, Decision Letter: Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Jan. 17, 2008), at 2.

[21] For example, in May 2001 FDA established a public docket (Docket No. 2001N-0103) to receive comment on whether pediatric exclusivity for an innovator runs concurrently or consecutively with 180-day exclusivity for the first generic applicant. 66 Fed. Reg. 27,983 (May 21, 2001).

[22] *See, e.g.*, Brenda Sandburg, *Generic Exclusivity Debate Continues at FDA: What Counts as a Forfeit?*, PINK SHEET, vol. 69, no. 43 (Oct. 22, 2007).

[23] FDA Law Blog, FDA Solicits Public Comment on Yet Another 180-Day Generic Drug Exclusivity Issue (Oct. 12, 2007), *available at* http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2007/10/fda-solicits-pu.html; Brenda Sandburg, *Generic Exclusivity Debate Continues at FDA: What Counts as a Forfeit?*, PINK SHEET, vol. 69, no. 43 (Oct. 22, 2007).

forfeiture provisions.[24] As discussed below in section III.B.4., however, there may be practical impediments to judicial resolution of forfeiture issues.

At least one FDA representative has defended the agency's practice of using nonrulemaking dockets to address complex issues by noting that the comments received in response to these solicitations have in general been more thoughtful than comments typically received in response to a notice of proposed rulemaking, because they were submitted by parties who had a real interest in the matters being considered.[25] Rulemaking may generate fewer thoughtful or helpful comments than would a nonrulemaking docket because generic manufacturers, who may at times be first applicants and at other times be subsequent applicants, depending on the circumstances, may be less inclined to take a position on an issue raised as part of a rulemaking that could affect first applicants and subsequent applicants differently.

Whether or not FDA's current practice of using nonrulemaking dockets to address interpretative issues, such as those arising under the forfeiture provisions, will weaken or bolster its position in court remains uncertain, as noted below in section III.B.4. It is likely, however, that as more ANDAs with paragraph IV certifications are filed under the new provisions, more interpretative issues will arise, particularly with respect to the forfeiture provisions. And at least for the time being, FDA has indicated that it plans to continue its practice of opening nonrulemaking dockets when facing these issues.[26]

In the sections that follow, the authors discuss the interpretive issues that arise for new ANDAs and old ANDAs, focusing heavily on developments since their last article. Section II discusses earning, maintaining, and triggering 180-day exclusivity. Section III discusses loss of eligibility and forfeiture. In section IV, the conclusion, the authors offer thoughts on the impact of 180-day exclusivity, topics on which legislation has been or might be proposed, and proposals for adoption of a similar model in a new context.

II. EARNING, MAINTAINING, AND TRIGGERING 180-DAY EXCLUSIVITY

A. *Earning and Maintaining Eligibility for Exclusivity*

1. *When must an ANDA applicant send notice of its paragraph IV certification to the innovator in order to earn 180-day exclusivity?*

Under the old provisions, 180-day exclusivity delayed approval of an ANDA with a paragraph IV certification if it was "for a drug for which a previous application [had] been submitted under [section 505(j) containing] such a certification." Prior to enactment of the MMA, this was interpreted to require that the first applicant

[24] For example, this observation was made by Robert A. Dormer at a FDLI conference on the Hatch-Waxman amendments on February 5, 2009. *See* Robert A. Dormer, *180-Day Exclusivity Forfeiture Mechanics, FDA Decisions, and Recent Court Decisions*, Presentation at FDLI's Waxman-Hatch: Back to the Future (Feb. 5, 2009) (stating that the "[t]rend of deciding on case-by-case basis often leaves it to the court to decide").

[25] This comment was made by Elizabeth Dickinson at a FDLI conference. *See supra* note 3.

[26] FDA, Decision Letter: Dorzolamide Hydrochloride/Timolol Maleate Tablets and 180-Day Exclusivity, Docket No. FDA-2008-N-0483-0001 (Oct. 28, 2008), at 1; FDA, Decision Letter: Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Jan. 17, 2008), at 1-2.

file a substantially complete ANDA with a paragraph IV certification and comply with both the certification and the notice provisions of section 505(j).

The pre-MMA statute was silent concerning when notice with respect to a paragraph IV certification in an original ANDA was required to be provided to the innovator. It stated, however, that notice regarding a paragraph IV certification in an amended ANDA was required to be "given when the amended application [was] submitted." FDA interpreted the timing requirement differently for amended ANDAs and for original ANDAs. With respect to an amended ANDA, FDA interpreted it to mean that notice was required simultaneously with the amended ANDA. Moreover, if the first applicant violated the notice provisions by providing notice *after* submitting the ANDA amendment, agency policy constructively moved the certification's filing date—and therefore the date on which the ANDA applicant could become eligible for 180-day exclusivity—to the day on which the applicant mailed the notice. This policy was sustained by the D.C. Circuit as a reasonable exercise of agency discretion.[27] In the case of an original ANDA, however, the agency referred to the certification date to determine when the applicant became eligible for exclusivity.[28] FDA's interpretation of when it considered notice to be provided for 180-day exclusivity purposes was articulated in 2003 and 2004 and is described in the authors' 2007 article.

Although Congress reworded the 180-day exclusivity provisions in 2003 and also amended the notice of certification provisions to specify the timing of providing such notice to the innovator, neither change affects the underlying requirement that the first applicant file a substantially complete ANDA with a paragraph IV certification and comply with both the certification and the notice provisions of section 505(j) to be eligible for 180-day exclusivity. Under the new provisions, 180-day exclusivity delays approval of an ANDA with a paragraph IV certification if that application is for "a drug for which a first applicant has submitted an application containing such a certification" (i.e., a drug for which someone else submitted an ANDA earning it eligibility for exclusivity). Congress also amended the notice provision to specify that a paragraph IV notice must be provided, in the case of an original ANDA, no later than 20 days after the date of the postmark on the

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[27] *See* Purepac Pharm. Co. v. Thompson, 354 F.3d 877 (D.C. Cir. 2004), *aff'g*, TorPharm, Inc. v. Thompson, 260 F. Supp. 2d 69 (D.D.C. 2003) (addressing FDA's interpretation of 21 U.S.C. § 355(j)(2)(B)(iii) and 21 C.F.R. § 314.95(d)).

[28] This became clear in a matter involving an ANDA filed in July 2002 by Purepac, seeking to market a generic version of Glucophage XR (metformin hydrochloride extended release). On November 5, 2002, the Patent and Trademark Office (PTO) issued a new patent claiming metformin hydrochloride. The patent was listed in the *Orange Book* on November 21. On November 5, and on every subsequent business day through November 25, Purepac submitted a paragraph IV certification to that patent. On November 27, Purepac sent notice of the paragraph IV certification to Bristol-Myers Squibb (BMS), the patent holder. BMS received that notice letter on December 3. IVAX filed an original ANDA after Purepac amended its ANDA, but before Purepac sent notice to BMS. IVAX included a paragraph IV certification to the second patent and notified BMS at that time. FDA awarded exclusivity to IVAX and not to Purepac, reasoning that the controlling dates for determination of first applicant status were Purepac's *notice* date (because Purepac was amending its ANDA) and IVAX's *certification* date (because IVAX was filing an original ANDA). Purepac filed a lawsuit against FDA, challenging the agency's award of exclusivity to IVAX. Purepac Pharm. Co. v. Thompson, No. 03-cv-02210 (D.D.C. Oct. 29, 2003) (complaint). IVAX intervened as a defendant. Purepac and IVAX subsequently settled the lawsuit by agreeing to share profits during the exclusivity period. *See IVAX, Purepac Settle Metformin 180-Day Generic Drug Exclusivity Suit*, FDA WEEK (Dec. 5, 2003); *Glucophage XR Settlement: Purepac, IVAX Split Generic Profits for 180 Days*, HEALTH NEWS DAILY (Nov. 28, 2003). Consequently, the judge dismissed the case on November 26. Purepac Pharm. Co. v. Thompson, No. 03-cv-02210 (D.D.C. Nov. 26, 2003) (consent order to dissolve temporary restraining order and stipulation of dismissal).

notice from FDA that the ANDA has been filed.[29] Congress did not change the statutory language stating that in the case of an ANDA amendment, notice of a paragraph IV certification must be provided when the generic applicant submits the amendment in question.[30]

As noted in the authors' 2007 article, IVAX and Mylan have argued that the change to the notice provision for original ANDAs signaled Congress's intent that the notice date should control in all cases, i.e., that the certification date should not control for purposes of eligibility for exclusivity with respect to either original or amended ANDAs. Both IVAX and Mylan submitted amendments containing paragraph IV certifications to their previously submitted ANDAs and contemporaneously sent notice to the NDA holders. Eon (in the IVAX matter) and Dr. Reddy's (in the Mylan matter) filed their original ANDAs containing paragraph IV certifications prior to the submission of IVAX and Mylan's amendments. Eon and Dr. Reddy's did not, however, submit their notices until after IVAX and Mylan submitted theirs. IVAX and Mylan asserted in separate petitions that the change in notice requirements in the MMA meant that to be eligible for 180-day exclusivity, the first applicant must submit a paragraph IV certification *and* satisfy the notice requirement, regardless of whether the certification was made in the original ANDA or an amendment to the ANDA.[31] IVAX withdrew its petition on September 15, 2006, and FDA approved the ANDA submitted by Eon (now known as Sandoz) on December 21, 2006.[32] In the Mylan matter, the district court upheld the validity and enforceability of the patent at issue and enjoined both Mylan and Dr. Reddy's from selling their generic products. The Federal Circuit affirmed the district court decision in the patent infringement litigation on May 11, 2007,[33] and denied a petition by Mylan for panel rehearing and rehearing en banc on June 19, 2007.[34] Mylan's citizen petition was subsequently withdrawn, presumably because it was no longer eligible for 180-day exclusivity in light of its unsuccessful patent challenge.[35] Although FDA did not respond to either petition, the agency apparently disagreed with the IVAX and Mylan interpretation of the effect of the changes to the notice requirement, because it awarded 180-day exclusivity to Eon in the IVAX matter.[36]

2. *Can more than one first applicant hold exclusivity with respect to one innovator drug?*

The issues of "multiple" and "shared" exclusivity can arise in three situations: 1) where multiple applicants submit ANDAs with paragraph IV certifications to different listed patents for the same innovator drug product; 2) where multiple

[29] 21 U.S.C. § 355(j)(2)(B)(ii)(I).

[30] 21 U.S.C. § 355(j)(2)(B)(ii)(II).

[31] IVAX, Citizen Petition, Docket No. 2004P-0520 (Nov. 19, 2004) (withdrawn); Mylan Pharmaceuticals, Inc., Citizen Petition, Docket No. 2006P-0245 (June 12, 2006) (withdrawn).

[32] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Sandoz, Inc. (Dec. 21, 2006).

[33] Janssen Pharmaceutica N.V. v Mylan Pharms., Inc., 223 Fed. Appx. 999 (Fed. Cir. 2007) (unpublished), *aff'g*, 456 F. Supp. 2d 644 (D.N.J. 2006).

[34] Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc., Nos. 2007-1021, 2007-1055, 2007 U.S. App. LEXIS 16041 (Fed. Cir. June 19, 2007).

[35] Mylan's letter, dated June 27, 2007, does not provide an explanation for its withdrawal of the citizen petition. The date of the letter suggests, however, that Mylan withdrew its petition in response to the Federal Circuit's June 19 decision.

[36] *See* Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Sandoz, Inc. (Dec. 21, 2006).

applicants submit ANDAs with paragraph IV certifications to the same patent or patents on the same first day; and 3) where multiple applicants submit ANDAs with paragraph IV certifications for different dosage forms or strengths of the same innovator drug. For old ANDAs, all three situations can result in more than one generic applicant holding 180-day exclusivity relating to a particular active ingredient. In particular, in the first situation, FDA interprets the statute as permitting patent-by-patent exclusivity, which can create multiple exclusivity periods for a product. Since the authors' last article, an appellate court has affirmed a decision finding this interpretation permissible. For new ANDAs, the first situation no longer leads to multiple exclusivity. In 2003, Congress provided that exclusivity should be awarded product by product, rather than patent by patent. The second and third situations can still lead to shared exclusivity.

a. *Different listed patents.*

In the late 1990s, FDA responded to two citizen petitions, stating that generic applicants who certify to different patents covering the same listed drug may hold exclusivity simultaneously.[37] American Pharmaceutical Partners (APP) and Pharmachemie had each requested that FDA stay approval of any ANDA other than its own for a generic version of Platinol-AQ (cisplatin injection). Pharmachemie had filed the first substantially complete ANDA with a paragraph IV certification to one patent listed for the product. The patent holder did not file suit, and the patent expired. APP had filed the first substantially complete ANDA with a paragraph IV certification to a different patent listed for the product. Pharmachemie then did the same thing. Bristol-Myers Squibb (BMS) filed suit against both companies, and each argued that it had been the first to file a paragraph IV certification for the drug. FDA defined the controversy as "whether multiple ANDA applicants each can be eligible for 180-day exclusivity because each applicant was the first to file a paragraph IV certification as to a different patent for the listed drug." The agency concluded that both applicants could be entitled to exclusivity. FDA stated that its regulations "direct that the inquiry is whether one or more substantially complete ANDAs were submitted that contained a certification that the same patent was invalid, not enforceable, or would not be infringed." Therefore, the agency wrote, "eligibility for exclusivity is to be determined on a patent-by-patent basis."[38]

Three subsequent court cases addressed FDA's view that eligibility for exclusivity was to be determined on a patent-by-patent basis. These cases were discussed in the authors' 2007 article. Two judges on the District Court for the District of Columbia ruled differently on the issue: one rejected the agency's approach and reversed the Agency in a case involving paroxetine,[39] and one found the agency's

[37] FDA, Response to APP and Pharmachemie Citizen Petitions, Docket No. 1999P-1271 (Aug. 2, 1999), at 4-5.

[38] FDA granted exclusivity only to APP, however, reasoning that Pharmachemie's exclusivity had terminated automatically when the patent for which Pharmachemie had submitted its paragraph IV certification expired. As noted in the 2007 article, FDA also addressed shared and multiple exclusivity in draft regulations published in 1999. 64 Fed. Reg. 42,873 (Aug. 6, 1999). Among other things, it proposed that exclusivity would be awarded product by product rather than patent by patent. The agency withdrew the proposal in 2002. 67 Fed. Reg. 66,593 (Nov. 1, 2002).

[39] TorPharm, Inc. v. FDA, No. 03-cv-2401, 2004 WL 64064 (D.D.C. Jan. 8, 2004) (written order memorializing oral order and judgment issued on Jan. 2). FDA appealed. Apotex, Inc. v. FDA, No. 03-cv-2401 (D.D.C. Feb. 6, 2004) (notice of appeal). The contested exclusivity period expired on March 6, 2004, and on December 17, 2004, the D.C. Circuit dismissed the appeal as moot. Apotex Inc. v. FDA, No. 04-5046 (D.C. Cir. Dec. 17, 2004) (judgment).

approach reasonable in a case involving gabapentin.[40] The issue has now been resolved in FDA's favor by the D.C. Circuit in a third case.

The D.C. Circuit case in question involved ANDAs for 40 mg versions of AstraZeneca's Prilosec (omeprazole). As the authors explained in 2007, the situation involved 11 listed patents and four generic applicants. FDA granted Andrx 180-day exclusivity on the basis that it was the first to file an ANDA for 40 mg omeprazole and to challenge six of the seven originally listed patents, only three of which were at issue in the exclusivity litigation. AstraZeneca brought suit against Andrx and other generic applicants for infringement of these three patents. Although the court found Andrx infringed two of the three patents at issue,[41] it granted summary judgment in favor of two of the other generic applicants on the third patent, holding it not infringed.[42] Accordingly, FDA could not make approval of the Andrx ANDA effective until expiry of the two infringed patents (and a pediatric exclusivity period) in October 2007. In addition, the ruling of non-infringement on the third patent triggered Andrx's 180-day exclusivity term with respect to that patent.

Andrx was also the first to challenge, in an amendment to its ANDA, four other patents listed by AstraZeneca after its original ANDA was submitted, making it eligible for a second exclusivity period under FDA's patent-by-patent approach. This exclusivity would begin to run when Andrx started commercial marketing—as noted, no earlier than October 2007. Apotex also filed an ANDA for the 40 mg strength, and it included paragraph IV certifications to, among others, the two patents that Andrx was found to infringe. Apotex then received tentative approval, but because of the second 180-day exclusivity term that Andrx would enjoy in 2007 (assuming FDA made its ANDA approval effective then), the soonest Apotex could enter the market with the 40 mg strength was April 2008.

Apotex brought suit against FDA, challenging the agency's patent-by-patent approach. The district court found section 505(j)(5)(B)(iv) ambiguous with respect to how many exclusivity periods may arise in connection with a single drug product, and it found FDA's patent-based approach "not entirely irrational."[43] Under the highly deferential standard of *Chevron USA, Inc. v. Natural Resources Defense Council, Inc.*,[44] therefore, the judge granted the agency's motion for summary judgment, thus upholding its patent-based approach. In February 2007, the D.C. Circuit affirmed.[45] Andrx's ANDA, which was acquired by Watson, was approved on May 30, 2008, and it was awarded a period of 180-day exclusivity with respect to the 40 mg strength.[46] For old ANDAs, therefore, 180-day exclusivity is awarded on a patent-by-patent basis.

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[40] Apotex Inc. v. FDA, 04-cv-00605 (D.D.C. June 3, 2004) (order); *see Court Split on FDA's Patent-by-Patent Approach to 180-Day Exclusivity*, FDA WEEK (June 11, 2004). The D.C. Circuit, however, concluded that *res judicata* barred Apotex from bringing suit and vacated the lower court's holding on the merits. Apotex v. FDA, 393 F.3d 210 (D.C. Cir. 2004). The case giving rise to *res judicata* was TorPharm, Inc. v. Thompson, 260 F. Supp. 2d 69 (D.D.C. 2003), which involved the same parties and the same ANDAs. That litigation related to FDA's decision to postpone the effective date of Purepac's certification to the second patent (rather than nullify it as TorPharm had argued).

[41] *See In re* Omeprazole Patent Litigation, 222 F. Supp. 2d 423 (S.D.N.Y. 2002), *aff'd*, 84 Fed. Appx. 76 (Fed. Cir. Dec. 11, 2003) (unpublished).

[42] *See* Apotex Inc. v. FDA, No. 05-cv-00125, 2005 WL 3568927, at 10 (D.D.C. Jan. 19, 2005) (complaint).

[43] Apotex Inc. v. FDA, 414 F. Supp. 2d 61 (D.D.C. 2006).

[44] 467 U.S. 837 (1984).

[45] Apotex Inc. v. FDA, 226 Fed. Appx. 4 (D.C. Cir. Feb. 23, 2007) (unpublished).

[46] Press Release, Watson, Watson Receives Final Approval of Omeprazole Delayed-Release Capsules (June 2, 2008), *available at* http://ir.watson.com/phoenix.zhtml?c=65778&p=irol-newsArticle&ID=1161090&highlight=.

With respect to new ANDAs, however, Congress established one 180-day exclusivity period per reference product. The new language precludes approval of an ANDA for 180 days after first commercial marketing by "any" first applicant.[47] A "first applicant" is "an applicant that, on the first day on which a substantially complete application containing a [paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug."[48] The provision also notes that if all first applicants forfeit exclusivity, "no applicant shall be eligible," which would be inconsistent with a patent-by-patent approach.[49]

b. *Same patents, same day.*

In August 2000, Zenith Goldline Pharmaceuticals petitioned FDA for a determination that "all [ANDAs] containing a paragraph IV certification delivered to FDA's Office of Generic Drugs (OGD) on the same business day are submitted at the same time for 180-day exclusivity purposes," each receiving 180-day exclusivity without being subject to the other's exclusivity.[50] In an accompanying petition, Zenith Goldline sought a stay of approval of a competitor's ANDA for alendronate sodium tablets—marketed by the innovator as Fosamax—until its own ANDA received approval.[51] On May 13, 2003, Ranbaxy Laboratories submitted a citizen petition making the same request with respect to generic versions of Provigil (modafinil).[52]

In July 2003, FDA issued a guidance document that permitted shared exclusivity in this situation and wrote both petitioners to explain that the guidance "essentially" granted their citizen petitions.[53] The agency explained that when, on the same day, more than one applicant submits an ANDA for the same drug containing a paragraph IV certification to a listed patent, and no such certification to the same patent was submitted previously, all the applicants will share exclusivity. The 180-day exclusivity would be triggered for all first applicants for a specific listed patent when one of them began to market its product (or on the date of any court decision finding that patent invalid, unenforceable, or not infringed, if earlier). The commercial marketing trigger would begin the 180-day exclusivity period as to all listed patents; a relevant court decision would trigger it only as to patents addressed in the decision.

The 2003 statutory language more clearly provides that when, on the same day, more than one applicant submits an ANDA for the same drug containing a paragraph IV certification to a listed patent, and no such certification was submitted previously, all the applicants will share exclusivity. As noted above, it precludes approval for 180 days after first commercial marketing by "any" first applicant[54]

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[47] 21 U.S.C. § 355(j)(5)(B)(iv)(I).

[48] 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb).

[49] 21 U.S.C. § 355(j)(5)(D)(iii)(II); *see also* 149 Cong. Rec. 31,783 (2003) (Sen. Kennedy) ("The Hatch-Waxman provisions in this bill also make the exclusivity available only with respect to the patent or patents challenged on the first day generic applicants challenge brand drug patents, which makes the exclusivity a product-by-product exclusivity rather than a patent-by-patent exclusivity.")

[50] Zenith Goldline Pharmaceuticals, Citizen Petition, Docket No. 2000P-1445 (Aug. 8, 2000).

[51] Zenith Goldline Pharmaceuticals, Petition for Stay of Action, Docket No. 2000P-1443 (Aug. 8, 2000).

[52] Ranbaxy Laboratories, Citizen Petition, Docket No. 2003P-0217 (May 13, 2003).

[53] FDA, Guidance for Industry, 180-Day Exclusivity When Multiple ANDAs Are Submitted on the Same Day (July 2003); FDA, Letter to IVAX Pharmaceuticals, Inc., Docket Nos. 2000P-1443 and 2000P-1445 (July 31, 2003); FDA, Letter to Venable, Baetjer, Howard & Civiletti LLP, Docket No. 2003P-0217 (July 31, 2003).

[54] 21 U.S.C. § 355(j)(5)(B)(vi)(I).

and precludes rollover if "all first applicants" forfeit their exclusivity.[55] It further clarifies who qualifies as a "first applicant" by adding a definition for the term, as discussed above in section I. B. Because Congress eliminated the court decision trigger, exclusivity will be triggered for all first applicants when one of them begins to market its product.

c. *Different dosage forms or strengths.*

In a 1999 decision involving generic copies of Zantac (ranitidine hydrochloride), the D.C. Circuit resolved in the affirmative the question whether applicants who market different dosages of a drug are eligible for separate 180-day exclusivity periods. Among the ranitidine hydrochloride products sold by Glaxo as Zantac were 150 mg and 300 mg tablets, both prescription drug products intended for the treatment of ulcers, and 75 mg tablets, sold over the counter (OTC) for the treatment of heartburn. Genpharm was the first to file an ANDA for the 150 mg and 300 mg tablets, and its exclusivity ran in 1997. FDA had since approved additional ANDAs for those strengths. Novopharm was the first to file an ANDA with a paragraph IV certification for a 75 mg OTC product and claimed it was therefore eligible for 180-day exclusivity. Apotex sought immediate approval of its own 75 mg tablets, however, on the theory that FDA may not grant separate exclusivity periods for ANDAs that concern patents listed with respect to previously approved drugs of different strengths. The district court disagreed, holding that permitting separate exclusivity periods for separate drug strengths is consistent with the statute, which requires that an ANDA contain, among other things, "information to show that the 'route of administration, the dosage form, and the *strength of the new drug* are the same as those of the listed drug.'"[56] For similar reasons, generic copies of tablet forms and capsule forms of the same drug are eligible for separate 180-day exclusivity periods.[57]

Although FDA has not addressed this issue with respect to new ANDAs, the requirement that exclusivity for new ANDAs be awarded product by product should lead to the same result.[58]

3. *What does it mean to "lawfully maintain" a paragraph IV certification?*

As noted above, for new ANDAs, the term "first applicant" means "an applicant that, on the first day on which a substantially complete application containing a

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[55] 21 U.S.C. § 355(j)(5)(D)(iii) (if all first applicants forfeit exclusivity, "no applicant shall be eligible").

[56] Apotex, Inc. v. Shalala, 53 F. Supp. 2d 454, 456 (D.D.C. 1999) (citation omitted) (emphasis added by the district court), *aff'd*, No. 99-5231, 1999 WL 956686 (D.C. Cir. Oct. 8, 1999).

[57] *See, e.g.*, Mylan Pharms., Inc. v. Shalala, 81 F. Supp. 2d 30, 35 n.8 (D.D.C. 2000) ("The tablet and capsule forms of the drug, however, are distinct products for FDCA purposes and are thus each eligible for their own exclusivity.")

[58] For example, in April 2004, Teva became the first applicant to submit an ANDA containing a paragraph IV certification to market generic Actonel (risedronate sodium) tablets in 5 mg, 30 mg, and 35 mg strengths. Teva's ANDA was granted approval on October 5, 2007, and it obtained 180-day exclusivity with respect to each strength according to the approval letter. FDA's list of paragraph IV certifications indicates that on September 10, 2007, the first substantially complete ANDA with a paragraph IV certification was filed for Actonel (risedronate sodium) tablets in the 75 mg strength. And on August 12, 2008, the first substantially complete ANDA with a paragraph IV certification for Actonel (risedronate sodium) tablets in the 150 mg strength was filed. Assuming these applicants do not forfeit exclusivity, if FDA continues the same policy as for the earlier applications for different strengths, they will presumably obtain 180-day exclusivity with respect to these other two strengths of this product.

[paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug."

Consequently, a new ANDA applicant that has first filer status cannot maintain its eligibility for 180-day exclusivity if it does not "lawfully maintain" its paragraph IV certification. One cannot "lawfully maintain" a patent challenge if one loses the ensuing litigation.[59] Thus, if an ANDA applicant loses a patent challenge (for example, to a drug substance patent), that patent challenge no longer qualifies the applicant for exclusivity. Moreover, the 75-day forfeiture clock begins to run as soon as the eligible applicant prevails on a different patent. Put another way, if the ANDA applicant challenges a formulation patent but adds a frivolous challenge to a drug substance patent, prevails on the formulation patent and loses on the substance patent, then the 75-day clock will begin to run. The generic applicant will forfeit exclusivity, if it cannot market within 75 days of the appellate decision on a patent it successfully challenged.[60]

4. *Are 180-day exclusivity rights waiveable?*

There have been no new developments with respect to this issue since the authors' last article. FDA developed a policy that the first filer may relinquish its exclusivity altogether at any time and may waive its 180-day exclusivity rights in favor of another specific generic applicant after exclusivity is triggered (meaning that the 180 days are running). Congress did not address this issue in 2003, and presumably this continues to be agency policy. Under the new provisions, exclusivity is triggered only by commercial marketing. It follows then that the first generic must launch its product before it can waive the exclusivity in favor of another applicant (also known as a "selective waiver").

In a 1997 case relating to generic copies of Zantac (ranitidine hydrochloride), a federal district court rejected a motion for a temporary restraining order (TRO), after FDA approved an ANDA filed by a second applicant who had purchased 180-day exclusivity from the first applicant.[61] The court noted that the Hatch-Waxman amendments are silent on the question of waiver of 180-day exclusivity, and FDA pointed to other instances where the agency had approved waivers with respect to five-year and three-year exclusivity under the Hatch-Waxman amendments. The court concluded that FDA's interpretation of the statute was not based on an impermissible construction of the statute, was neither arbitrary nor capricious, and was not an abuse of discretion. It therefore denied emergency relief.

In proposed regulations published in 1999, FDA restated its position that 180-day exclusivity rights may be waived.[62] Under one part of this proposal, once a subsequent generic applicant received tentative approval for its generic drug from FDA (such that the exclusivity was the only obstacle to final approval), a triggering period would begin to run. Within 180 days, one of the two triggering events

[59] *See* 21 C.F.R. § 314.94(a)(12)(viii)(A) ("An applicant who has submitted a [paragraph IV certification] and is sued for patent infringement within 45 days of the receipt of notice ... shall amend the certification [to a paragraph III] if a final judgment in the action against the applicant is entered finding the patent to be infringed.")

[60] As the authors explained in 2007, this precludes a generic applicant from "parking" exclusivity—blocking subsequent ANDA applicants—by challenging two patents, knowing that the company will lose on the patent that is not due to expire for some time.

[61] Boehringer Ingelheim Corp. v. Shalala, 993 F. Supp.1 (D.D.C. 1997).

[62] 64 Fed. Reg. 42,873, 42,881 (Aug. 6, 1999).

for the exclusivity period to run—a favorable court decision regarding the patent or commercial marketing by the first applicant—would need to occur, or the first generic would lose its exclusivity. After a triggering event occurred, the first generic would be permitted to waive its rights in favor of another company. FDA noted that waiver can be particularly useful when a subsequent generic wins its patent suit with the innovator before the first generic's suit goes to trial. Prior to the triggering event, however, the first generic could not waive its exclusivity rights. It could relinquish its rights—waive its exclusivity entirely—permitting FDA to approve all subsequent ANDAs, but it could not sell the exclusivity term to a particular generic manufacturer. FDA withdrew its proposed regulations in 2002, but confirmed this position two years later in response to a Pfizer citizen petition.[63]

On May 11, 2004, Pfizer submitted a citizen petition to FDA asking the agency to acknowledge that 180-day exclusivity cannot lawfully be waived or transferred.[64] Pfizer argued, among other things, that the plain language of the statute does not permit waiver or transfer and that permitting exclusivity to be fully alienable encourages ANDA applicants to file weak applications simply to vest a lucrative asset. On July 2, 2004, the agency denied that citizen petition.[65] FDA rejected the textual argument on the ground that section 505(j)(5)(B)(iv) is ambiguous and can reasonably be interpreted to permit waiver. Further, the agency added, the statute confers a private benefit to specific entities, and in such situations judicial precedent supports inferring that the agency may allow an alternative course of action more favorable to the beneficiary. Finally, the agency noted, allowing generic applicants to waive their exclusivity promotes competition by enabling other generic applicants to market their products sooner.

FDA's response makes it clear that the agency continues to require a triggering event in order to distinguish between relinquishment and selective waiver. "As to potential 'gaming,' if the first applicant could selectively waive its exclusivity at any time," FDA wrote, the agency "could reasonably expect the development of a 'market' for 180-day exclusivity, with a resulting increase in ANDA's submitted solely to claim exclusivity." FDA concluded, however, "that by permitting selective waiver only once the exclusivity is triggered, it can prevent 'gaming' of exclusivity, avoid unnecessary exclusivity disputes, and still maintain exclusivity as an adequate incentive and reward."

5. *Does 180-day exclusivity roll over to a subsequent applicant in the event that the first applicant forfeits, or does not perfect, its rights?*

There have been no developments regarding this issue since the authors' 2007 article. The agency consistently took the position that exclusivity would not roll over to a second applicant under the language applicable to old ANDAs, and the 2003 legislation explicitly rejects roll-over for new ANDAs.

Prior to 1999, there were no cases or official FDA pronouncements on the question whether exclusivity might roll over to a second applicant. The agency did note in 1994 that if the first applicant was "not actively pursuing approval" of its ANDA,

[63] In the interim, in a 2000 case involving Hytrin (terozosin), a district court wrote that "exclusivity periods are a transferable commodity which can be waived in favor of another generic manufacturer for a substantial price." Mylan Pharm., Inc. v. Shalala, 81 F. Supp. 2d 30, 42 (D.D.C. 2000).

[64] Pfizer, Inc., Citizen Petition, Docket No. 2004P-0227 (May 11, 2004).

[65] FDA, Response to Pfizer Citizen Petition, Docket No. 2004P-0227 (July 2, 2004).

FDA would make approval of subsequent ANDAs immediately effective.[66] But the 1999 proposed regulations addressed the issue directly. The agency stated that, in order to be entitled to 180-day exclusivity, an ANDA applicant needed to be the first to file a substantially complete ANDA with a paragraph IV certification.[67] An ANDA was not substantially complete if FDA determined that the required bioequivalence data failed to meet FDA standards. If FDA found the bioequivalence studies to be deficient, that applicant would lose its exclusivity, and no other applicant would be granted exclusivity. FDA noted that, as this suggests, there would be no "rolling exclusivity." Thus, for example, if the first generic withdrew its application or was found by a court to be infringing the patent, exclusivity would not roll over to the next-filed ANDA. The 2003 legislation requires the same result for new ANDAs; as noted in section I. B. if all first applicants forfeit exclusivity, "no applicant shall be eligible."[68]

B. *Court Decision Trigger*

As discussed above, there is a court decision trigger for exclusivity only with respect to old ANDAs. The discussion that follows is therefore primarily relevant for the handful of products with ANDAs pending at the agency that are subject to the old provisions. But because there is a court decision trigger for forfeiture under the new provision, some of the agency's thinking and experience with respect to the court decision trigger for exclusivity may be instructive for new ANDAs.

1. *Must the first applicant have itself been sued for patent infringement, and must it have itself prevailed in that patent infringement litigation, in order to obtain the benefit of 180-day exclusivity?*

Although the agency initially concluded that a first generic would be eligible for exclusivity only if it had been sued for patent infringement and prevailed, the D.C. Circuit decided otherwise in 1998. For old ANDAs, there is no suit or "successful defense" requirement. Another generic can be sued and prevail instead, triggering the exclusivity, or the case can be dismissed. There have been no developments on this issue since the 2007 article.

When FDA initially proposed regulations to implement 180-day exclusivity, it stated that a generic applicant was entitled to exclusivity only when it had itself been sued for patent infringement and prevailed in that lawsuit. It stated that to permit otherwise "would provide a windfall to an applicant who has not devoted the considerable time and money necessary for patent litigation."[69] After the Commissioner of Food and Drugs signed the *Federal Register* notice of the proposed regulations, but before publication of the proposal in the *Federal Register*, a federal district court reached a contrary conclusion on the issue whether the generic applicant must have been sued, itself, by the patent holder.

In this case, involving generic copies of Inderal (propranolol hydrochloride), the district court noted that the "alternatives are clear"—the "primary ANDA

[66] 59 Fed. Reg. 50,338, 50,367-50,368 (Oct. 3, 1994).
[67] 64 Fed. Reg. 42,873, 42,875 (Aug. 6, 1999).
[68] 21 U.S.C. § 355(j)(5)(D)(iii).
[69] 59 Fed. Reg. 50,338, 50,353 (Oct. 3, 1994).

applicant can qualify for exclusivity beginning *either* on the date of a court decision invalidating a patent or holding that it is not infringed *or* on the date of first commercial marketing of the applicant's product."[70] "There is no ambiguity" in the statute, the court wrote, "that requires the Court or permits the FDA to read into it a requirement of a lawsuit which is simply not there." The agency appealed the decision, however, and the case was dismissed as moot before FDA concluded the rulemaking.[71]

In its final regulations, published in 1994, the agency stood by its earlier position. A generic applicant would be entitled to exclusivity only if it had successfully defended a patent infringement suit. Neither the court decision nor the commercial marketing trigger would apply, unless and until the first applicant won its patent infringement suit. FDA believed that to provide otherwise would "create[] an incentive for frivolous claims of patent invalidity or noninfringement."[72]

In 1998, the agency's position was invalidated. In December 1994, Mova filed an ANDA with a paragraph IV certification to market a generic version of Micronase (micronized glyburide), a diabetes drug marketed by Pharmacia. Pharmacia sued Mova for infringing its patent. In November 1995, while Mova was engaged in that litigation, Mylan filed an ANDA for the same product and eventually filed a paragraph IV certification. Pharmacia declined to sue, and FDA approved Mylan's application on December 19, 1996. FDA reasoned that Mova's exclusivity did not bar approval of the Mylan ANDA, because Mova had not yet successfully defended against Pharmacia's suit. Mova then brought suit to compel FDA to delay the effective date of its approval of Mylan's product until 180 days after the earlier of the date Mova won its lawsuit or the date it began to market its product. Mova challenged the successful defense regulation as contrary to the plain language of the statute. The district court found that Mova had a very high likelihood of success on the merits of its claim and granted a preliminary injunction.[73]

In 1998, the D.C. Circuit affirmed that holding.[74] Although FDA argued that its successful defense requirement furthered the intent of Congress, the court disagreed. The successful defense requirement, the court wrote, is "gravely inconsistent with the text and structure of the statute." The D.C. Circuit explained, "[t]he commercial-marketing trigger seems intended to insure that, if a first ANDA applicant chooses to begin marketing its product before it has won its patent-infringement suit, the 180-day exclusivity period will begin to run immediately. Under the FDA's regulation, however, the 180-day exclusivity period is only available to an applicant who has *already* 'successfully defended against a suit for patent infringement.'" Its practical effect, the court wrote, is "to write the commercial-marketing trigger out of the statute."[75] The court recognized the issue, raised by Mylan, that the statutory scheme might penalize a meritorious second ANDA applicant. Nevertheless, the

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[70] Inwood Labs., Inc. v. Young, 723 F. Supp. 1523, 1526 (D.D.C. 1989), *vacated as moot*, No. 89-5209 (D.C. Cir. Nov. 13, 1989).

[71] Inwood asked the court of appeals to declare the case moot when six months had elapsed after the lower court enjoined FDA from approving another ANDA. *See Inwood Case May Not Set Precedent on Exclusivity*, WASH. DRUG LETTER (Oct. 30, 1989), at 2.

[72] 59 Fed. Reg. 50,338, 50,353 (Oct. 3, 1994).

[73] Mova Pharm. Corp. v. Shalala, 955 F. Supp. 128 (D.D.C. 1997).

[74] Mova Pharm. Corp. v. Shalala, 140 F.3d 1060 (D.C. Cir. 1998).

[75] *Id.* at 1069-1070. The court reasoned that "if the first applicant begins marketing its product before it wins its infringement suit, the 180 days of exclusivity do not begin to run; other applicants remain eligible for FDA approval to begin marketing their products, at least up to the date that the first applicant wins the infringement action." *Id.* at 1070.

court found that the successful defense requirement was too "blunt an instrument" to address that issue. The regulation was, thus, invalid. As explained in the authors' 2007 article, the Fourth Circuit reached the same conclusion in an unpublished case earlier the same year.[76]

Shortly after these decisions, FDA issued a guidance announcing its intent to remove the successful defense requirement from the regulation and to issue new regulations.[77] In the meantime, FDA stated, it would "regulate directly from the statute" and "make decisions on 180-day generic drug exclusivity on a case-by-case basis." The agency would inform the first applicant to submit a substantially complete abbreviated application with a paragraph IV certification that it was eligible for 180 days of exclusivity even though it had not been sued for patent infringement. In November 1998, FDA published an interim rule, eliminating the successful defense requirement.[78]

Later the same year, the D.C. Circuit approved FDA's new approach, noting that the first generic need not be sued for patent infringement to be eligible for exclusivity. TorPharm was the first to file an ANDA for a generic version of Ticlid (ticlopidine hydrochloride). Its ANDA contained a paragraph IV certification. The patent owner did not file suit against TorPharm. FDA tentatively approved an ANDA filed by Purepac, but because the agency had not given final approval to TorPharm and there was not a qualifying court decision, TorPharm's exclusivity had not begun to run. Accordingly, FDA withheld final approval of Purepac's ANDA pending TorPharm's final approval, commercial marketing, and expiry of its 180-day exclusivity. Purepac sued FDA seeking an injunction claiming that TorPharm was not entitled to exclusivity because it had not been sued for infringement. Consistent with the *Mova* decision and its new guidance, the agency responded that a suit was not required. The D.C. Circuit agreed, concluding that FDA's revised approach was consistent with the statute and the *Mova* decision, noting that the statute "does not, on its face, require the first applicant to be sued in order to benefit from" 180-day exclusivity.[79] Thus, FDA could withhold final approval of the Purepac ANDA until TorPharm had commercially marketed for 180 days.

Although there is no successful defense requirement, if the first applicant loses the patent infringement case, it must amend its certification to a paragraph III certification, and it is no longer eligible for exclusivity. This was made clear in a 2000 lawsuit involving the old statutory provisions and generic tamoxifen, and presumably it also applies to new ANDAs. The Southern District of New York had invalidated the innovator's patent, but that decision was subsequently appealed and vacated pursuant to a settlement agreement between the innovator, Imperial Chemical Industries, and the generic manufacturer, Barr. Also pursuant to the settlement, Barr amended its ANDA to change from a paragraph IV to a paragraph III certification. In addition, Barr obtained a license to market the product prior to patent expiry. FDA declined to treat the New York decision as a "court decision" for purposes of exclusivity and instead agreed with Barr that its exclusivity was intact. Mylan, a subsequent filer, sued FDA. The district court held that Barr had waived its eligibility for 180-day exclusivity, explaining that once a company changes its certification, the ANDA is no longer considered to have "contained" a

[76] Granutec, Inc. v. Shalala, 139 F.3d 889 (4th Cir. 1998) (unpublished).

[77] *See* FDA, Guidance for Industry, 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the FDCA (June 1998).

[78] 63 Fed. Reg. 59,710 (Nov. 5, 1998).

[79] Purepac Pharm. Co. v. Friedman, 162 F.3d 1201, 1204 (D.C. Cir. 1998).

paragraph IV certification.[80] This meant Barr was no longer eligible for exclusivity, and because FDA took the position that there was no rolling exclusivity under the statute, the agency could approve Mylan's ANDA.

2. *What kind of court decision triggers 180-day exclusivity?*

In April 2006, following litigation involving generic copies of Pravachol (pravastatin sodium), FDA announced a policy that the court decision trigger applicable to old ANDAs requires a decision of a court that on its face evidences a holding on the merits of patent non-infringement, invalidity, or unenforceability. Although to the authors' knowledge the issue has not yet arisen, the agency may apply the same policy to court decisions triggering forfeiture under the new statutory provisions. There is no court decision trigger for exclusivity for new ANDAs.

a. *Ticlid (ticlopidine) decision.*

As noted above, TorPharm was the first to file an ANDA for ticlopidine hydrochloride, a generic version of Ticlid. Teva Pharmaceuticals filed a subsequent ANDA, and it was not sued for patent infringement. Teva sued the patent owner, Syntex, in the Northern District of California, seeking a declaratory judgment of non-infringement. As explained later by the D.C. Circuit, the California court "dismissed the complaint for lack of subject-matter jurisdiction after finding, based on the patent holder's admission of non-infringement, that Teva lacked a reasonable apprehension of suit by the patent holder."[81]

In October 1998, FDA tentatively approved Teva's ANDA. FDA informed Teva, however, that because there was a prior ANDA applicant and neither commercial marketing nor a relevant court decision had occurred, Teva's application was ineligible for final approval. Teva argued to FDA, to no avail, that the California court's dismissal of its declaratory judgment suit against Syntex satisfied the "court decision" requirement, triggering TorPharm's exclusivity. Teva then brought suit in federal district court in the District of Columbia, seeking to have its ANDA approved effective 180 days after the California court dismissed the declaratory judgment suit. The district court upheld FDA's decision and denied injunctive relief. The D.C. Circuit reversed, holding that FDA's unexplained refusal to recognize dismissal by the California court as the functional equivalent of a final decision of non-infringement was arbitrary.[82] The court cited several reasons in support of its ruling, including that "[a] 'decision' can take several forms, including final judgment after a full trial, summary judgment or partial summary judgment, or even dismissal for failure to state a cause of action."

Following this decision, FDA provided a rationale for refusing to recognize dismissal of Teva's declaratory judgment action as a triggering court decision. FDA explained that generic applicants seeking to avail themselves of the court decision trigger must submit a copy of the court decision in question. The agency would not review any additional papers from the underlying litigation. The reason for Teva's dismissal "was not evident from the face of the court order, [and] the court did not issue a memorandum opinion explaining the basis for the order." Requiring staff in the OGD to delve beyond these documents would "place an unbearable burden" on the office. On remand, however, the district court rejected

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[80] *See* Mylan Pharms. Inc. v. Henney, 94 F. Supp. 2d 36 (D.D.C. 2000), *vacated and dismissed as moot*, Pharmachemie B.V. v. Barr Labs., Inc., 276 F.3d 627 (D.C. Cir. 2002).

[81] Teva Pharms., USA, Inc. v. FDA, 182 F.3d 1003, 1004 (D.C. Cir. 1999).

[82] *See id.* at 1007-1008.

FDA's explanation, noting—among other things—that "this is not a case where a great deal of sophisticated legal analysis is required."[83]

b. *Pravachol (pravastatin sodium) decision.*

In December 2000, Teva filed the first ANDA to market generic copies of Pravachol (pravastatin sodium) in 10 mg, 20 mg, and 40 mg tablets. Teva included a paragraph III certification for the patent on the molecule and paragraph IV certifications for certain other listed patents. The NDA holder, BMS, did not sue Teva or any of the other generic drug manufacturers that filed applications with paragraph IV certifications. FDA tentatively approved Teva's ANDA (pending expiry of the patent on the molecule) in May 2002. One of the other generic applicants, Apotex, sued BMS in October 2003, seeking a declaratory judgment that the patents in question were invalid or not infringed by it.

In July 2004, the court entered a "stipulation and order," signed by both parties, stating that BMS had "no intention to bring suit against Apotex for infringement."[84] Apotex returned to FDA, asking that it find this to be a "court decision" that triggered Teva's exclusivity. FDA agreed, apparently concluding that the decision in the ticlopidine case meant any dismissal of a declaratory judgment case triggers exclusivity.

This meant Teva's exclusivity would run before the patent expired for which Teva had submitted a paragraph III certification, so Teva brought suit. In March 2006, the D.C. Circuit rejected FDA's reading of the ticlopidine decision. It explained that, in the ticlopidine case, "the court stated that the statute *could* be interpreted to include dismissals of declaratory judgment actions as triggering events," but "it left the final decision to the FDA."[85] In short, the ticlodipine court had simply found the trigger ambiguous. The agency "mistakenly thought itself bound," which "renders its decision arbitrary and capricious." Thus, "[w]hile the statute may preclude treating voluntary dismissals ... as triggering events, we express no opinion on the matter." Instead, it is "up to the agency to ... make a reasonable policy choice," and "FDA has not yet done so."[86]

The agency responded to this court decision in an April 2006 letter to Apotex and the other generic applicants, stating that "FDA interprets the court decision trigger provision to require a decision of a court that on its face evidences a holding on the merits of patent non-infringement, invalidity, or unenforceability."[87] In the pravastatin case, therefore, Teva's exclusivity period had not been triggered by the July 2004 dismissal of the Apotex litigation. Following another rush of litigation by Apotex (a request for injunction and then appeal to the D.C. Circuit),[88] FDA granted Teva final approval on April 24.[89] Apotex obtained final approval six months later on October 23.

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[83] Teva Pharms. USA, Inc. v. FDA, No. 99-cv-00067, 1999 WL 1042743, at *5 (D.D.C. Aug. 19, 1999), *aff'd*, 254 F.3d 316 (D.C. Cir. 2000) (unpublished).

[84] Apotex Inc. v. Bristol-Myers Squibb Co., No. 04-cv-02922, at 3 (S.D.N.Y. July 23, 2004) (stipulation and order).

[85] Teva Pharms., USA, Inc. v. FDA, 441 F.3d 1, 4 (D.C. Cir. 2006).

[86] *Id.* at 5.

[87] *See* Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Pravastatin ANDA Applicant 15 (Apr. 11, 2006), *available at* www.fda.gov/cder/ogd/announce/Pravastatin-180Day-amend.pdf.

[88] *See* Apotex Inc. v. FDA, No. 06-00627 (D.D.C. Apr. 19, 2006) (denying motions for a TRO and a preliminary injunction); No. 06-5105 (D.C. Cir. Apr. 20, 2006) (granting emergency motion for injunctive relief—issuing administrative injunction—pending further order of the court); No. 06-5105 (D.C. Cir. Apr. 24, 2006) (dissolving administrative injunction and denying motion for injunctive relief pending appeal); 449 F.3d 1249 (D.C. Cir. 2006) (summarily affirming district court's refusal to grant preliminary injunction); No. 06-1505, 2006 U.S. App. LEXIS 21363 (D.C. Cir. Aug. 17, 2006) (denying request for rehearing en banc).

[89] Dana Elfin, *FDA Approves Teva's Generic Pravastatin, As Court Denies Apotex Emergency Relief*, 4 PHARM. LAW & INDUS. REPORT 499 (2006).

c. *Zofran (ondansetron hydrochloride) decision.*

In June 2001, Dr. Reddy's became the first applicant to file an ANDA containing paragraph IV certifications to the '789 and '658 patents claiming GlaxoSmithKline's (GSK's) Zofran (ondansetron hydrochloride) tablets.[90] GSK brought suit against Dr. Reddy's with respect to the '789 patent.[91] According to FDA, the parties subsequently entered into a settlement agreement under which Dr. Reddy's agreed to amend its certification with respect to the '789 patent from a paragraph IV to a paragraph III and thus not market its generic product prior to December 24, 2006, the expiration of pediatric exclusivity attached to the patent.[92]

In the meantime, Apotex and Mutual filed ANDAs seeking to market ondansetron hydrochloride tablets and included paragraph IV certifications to the '658 patent. With respect to Mutual, GSK did not bring an infringement action within 45 days after receiving notice of Mutual's certification, and the generic applicant filed an action against GSK to obtain a declaratory judgment of noninfringement of the patent.[93] The court noted that GSK subsequently stipulated to non-infringement of the '658 patent and covenanted not to sue Mutual for infringement of the patent, and the court dismissed the case with prejudice.[94] With respect to Apotex, GSK brought a lawsuit alleging infringement of the '658 patent.[95] The case was dismissed with prejudice after GSK stipulated to non-infringement and covenanted not to sue Apotex for infringement.[96]

In separate letters to FDA, Mutual and Apotex argued that the stipulated dismissals of their respective cases satisfied FDA's "holding-on-the-merits" policy and thus constituted court decision triggers for purposes of starting Dr. Reddy's 180-day exclusivity.[97] FDA denied both requests in November 2006.[98] The agency explained that in neither case did the district court resolve the dispute on the merits. Consequently, the stipulated dismissals did not reflect a holding on the merits of the patent claims at issue and thus did not satisfy FDA's court decision trigger

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[90] GSK listed two other patents in the *Orange Book* with respect to Zofran. These patents were not at issue.

[91] Glaxo Group Ltd. v. Dr. Reddy's Labs. Ltd., No. 01-4066 (D.N.J. Aug. 24, 2001) (complaint).

[92] Letter from Gary Buehler, Director, FDA Office of Generic Drugs to Dr. Reddy's Laboratories, Inc. 2 (Dec. 26, 2006).

[93] Mutual Pharm, Co., Inc. v. Glaxo Group Ltd., No. 03-cv-00426 (E.D. Va. May 14, 2003) (complaint).

[94] Mutual Pharm, Co., Inc. v. Glaxo Group Ltd., No. 03-cv-00426 (E.D. Va. July 18, 2003) (stipulation of dismissal).

[95] Glaxo Group Ltd. v. Apotex, Inc., No.05-307 (D.N.J. Jan. 14, 2005) (complaint).

[96] Glaxo Group Ltd. v. Apotex, Inc., No.05-307 (D.N.J. May 25, 2005) (stipulation and order of dismissal).

[97] Letter from Robert Dettery, Vice-President, Regulatory Affairs, Mutual Pharmaceutical Co., Inc., to Gary Buehler, Director, FDA Office of Generic Drugs (June 23, 2006); Letter from Christine J. Siwik and William A. Rakoczy, Rakoczy Molino Mazzochi Siwik LLP, to Gary Buehler, Director, FDA Office of Generic Drugs (Aug, 29, 2006). Mutual and Apotex made similar requests in letters sent to FDA prior to the agency's April 11, 2006 announcement of the holding-on-the-merits standard, discussed previously. *See* Letter from Robert Dettery, Vice-President, Regulatory Affairs, Mutual Pharmaceutical Co., Inc., to Gary Buehler, Director, FDA Office of Generic Drugs (Aug. 6, 2003); Letter from Christine J. Siwik and William A. Rakoczy, Rakoczy Molino Mazzochi Siwik LLP, to Gary Buehler, Director, FDA Office of Generic Drugs (Aug, 31, 2005).

[98] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Christine J. Siwik and William A. Rakoczy, Rakoczy Molino Mazzochi Siwik LLP (Nov. 3, 2006); Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Robert Dettery, Mutual Pharmaceutical Co., Inc. (Nov. 8, 2006).

policy. Although Apotex brought suit,[99] its motion for a preliminary injunction was denied without an opinion, and the D.C. Circuit summarily affirmed.[100]

d. *Medicare Modernization Act.*

In 2003, Congress eliminated the court decision trigger for 180-day exclusivity. For new ANDAs, exclusivity begins with the first commercial marketing of the drug product by a first applicant. Although Congress eliminated the court decision trigger for beginning the period of exclusivity, it established a new court decision trigger for forfeiture of exclusivity. Once the first generic applicant obtains final approval of its ANDA, its exclusivity does not begin to run until it commercially markets. Moreover, unless another forfeiture provision applies, that exclusivity is not forfeited until 75 days after a court decision on every patent qualifying it for exclusivity (assuming the first prong of the failure to market provision has been triggered). The legislative history contains a reference to the ticlopidine case,[101] suggesting that at least one member of the Senate viewed a decision dismissing a declaratory judgment action for lack of subject matter jurisdiction because the patent owner has represented that the patent is not infringed as a court decision triggering forfeiture. But the pravastatin court questioned that reading of the ticlodipine decision, and the agency's subsequently announced policy is more narrow.[102] It remains to be seen whether FDA will apply the April 2006 policy to court decisions triggering forfeiture or whether it will instead revert to its earlier interpretation of the ticlodipine case.

3. *What level of court decision triggers 180-day exclusivity?*

There have been no developments in this area since the authors last wrote. The 2003 legislation addressed the issue retroactively for old ANDAs; exclusivity begins when a decision is rendered by "a court from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken."[103] There is no court decision trigger for exclusivity for new ANDAs, but the same language appears with respect to the court decision forfeiture event.

a. *Old ANDAs.*

In the preamble to its final 1994 regulations, FDA stated that the court decision activating the court decision trigger "must be a final decision from which no appeal can be or has been taken."[104] This was rejected in a January 2000 case involving generic copies of Hytrin (terazosin hydrochloride). The district court rejected FDA's position that the triggering event is "either the date that a district court decision is

[99] Apotex requested that the court set aside the agency's decision, declare that the agency's refusal to treat the dismissal order as a triggering court decision was arbitrary, and direct FDA to approve Apotex's ANDA on December 24, 2006. Apotex Inc. v. FDA, No. 06-cv-1890, at 2 (D.D.C. Nov. 6, 2006) (complaint).

[100] Apotex Inc. v. FDA, No. 06-5408 (D.C. Cir. Dec. 22, 2006) (order). Shortly thereafter, the parties stipulated to a voluntary dismissal of the case with prejudice. Apotex Inc. v. FDA, No. 06-cv-1890 (D.D.C. Feb. 28, 2007) (stipulation of dismissal).

[101] *See* 149 Cong. Rec. 31,783 (2003) (Sen. Kennedy) ("We do intend that a court decision like the one in the D.C. Circuit's 1999 decision in *Teva v. Shalala*—a decision dismissing a declaratory judgment action for lack of subject matter jurisdiction because the patent owner has represented that the patent is not infringed—will count as a court decision under the new 'failure to market' provision.").

[102] *See* Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Pravastatin ANDA Applicant 15 (Apr. 11, 2006), *available at* www.fda.gov/cder/ogd/announce/Pravastatin-180Day-amend.pdf.

[103] Pub. L. No. 108-173 § 1102(b)(3), 117 Stat. 2066, 2460 (2003).

[104] 59 Fed. Reg. 50,338, 50,354 (Oct. 3, 1994).

affirmed by the Federal Circuit, or the date on which the time for filing an appeal has lapsed." In other words, "decision of a court" included "the decision of a United States district court regardless of whether that decision is appealed."[105]

In March 2000, FDA issued a guidance document implementing this court decision,[106] and shortly afterwards, the agency published interim regulations amending the definition of "court decision" to be consistent with its guidance and the terazosin decision.[107] The agency agreed that this new interpretation could compromise companies that had developed marketing strategies in reliance on the old definition of court decision; it could put them in the position of exposing themselves to damages if they were to market their products (to take advantage of the 180-day period) but lose in the appeal of the patent case. The agency concluded that the new definition of court would therefore apply only to ANDAs filed after March 30, 2000.

Congress reversed the rule in 2003, however, and this is one of two topics on which the 2003 legislation is retroactive. Exclusivity for old ANDAs begins when a decision is rendered by "a court from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken."[108]

b. *New ANDAs.*

There is no court decision trigger for exclusivity for new ANDAs, although (as discussed in more detail below, see III. A. 1), there is a court decision trigger for forfeiture of exclusivity.

4. *Under what circumstances may a subsequent applicant bring a declaratory judgment suit against the innovator or patent holder in order to trigger the first applicant's exclusivity?*

The court decision trigger for exclusivity under the old ANDA provisions was interpreted to permit a subsequent ANDA applicant to trigger the first ANDA applicant's 180-day exclusivity by prevailing in its own court case, clearing the way for the subsequent applicant that triggered the exclusivity (and other applicants) to market after expiry of the exclusivity. Where the innovator had not sued the subsequent applicant for patent infringement on at least one of the patents for which a paragraph IV certification was submitted, that applicant sometimes sought the triggering court decision itself through a declaratory judgment suit against the

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[105] Mylan Pharms., Inc. v. Shalala, 81 F. Supp. 2d 30, 47 (D.D.C. 2000).

[106] FDA, Guidance for Industry, Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the FDCA (Mar. 2000). The agency stated that it would interpret the term "court" to mean "the first court that renders a decision finding the patent at issue invalid, unenforceable, or not infringed." It would apply this to both 30-month stays and 180-day exclusivity. Thus, if a district court rendered such a decision, the 30-month stay would end for that ANDA as of the date the district court entered its decision, and 180-day exclusivity for the first filer would also begin to run on that date (unless it had begun already with commercial marketing). Neither a stay nor a reversal of this decision would lead to revocation of approval of that ANDA or the first filer's 180-day exclusivity. If a district court found patent infringement, however, and that ruling was reversed by the Federal Circuit, that generic's ANDA would be approved, and the 180-day exclusivity would start "on the date the district court issues a judgment that the patent is invalid, unenforceable, or not infringed pursuant to a mandate issued by a court of appeals."

[107] 65 Fed. Reg. 43,233 (July 13, 2000).

[108] Pub. L. No. 108-173 § 1102(b)(3), 117 Stat. 2066, 2460 (2003). By way of contrast, Congress provided in 2003 that 30-month stays for new ANDAs would end with a district court decision. Thus, district court decisions will end 30-month stays but not trigger the running of 180-day exclusivity. If the 30-month stay ends, however, and FDA approves the ANDA, any commercial marketing under the ANDA will trigger 180-day exclusivity for old ANDAs or new ANDAs.

innovator.[109] And although there is no court decision trigger for exclusivity under the new provisions, there is a court decision trigger for forfeiture, which has led subsequent ANDA applicants similarly to seek declaratory judgment to cause forfeiture of the exclusivity that is blocking them from the market.[110] Although the authors did not discuss this issue in the last article, there have been significant developments on the question whether and when an ANDA applicant that has not itself been sued with respect to all of the challenged patents can satisfy the constitutional "case or controversy" requirement in order to bring a declaratory judgment case in federal court. The issue continues to play out in the lower courts in cases brought by applicants seeking to trigger forfeiture, so it is worth a short mention in this article.

Prior to January 2007, courts determining whether there was jurisdiction to hear a declaratory judgment action concerning a patent applied the Federal Circuit's "reasonable apprehension of suit" test to determine whether a declaratory judgment plaintiff satisfied the case or controversy requirement.[111] The reasonable apprehension of suit test required that a party seeking declaratory relief establish an explicit threat or other action by the patentee, creating a reasonable apprehension on the part of the declaratory judgment plaintiff that it would face an infringement suit.[112] Applying this test, courts generally took the position that in the absence of some overt action demonstrating a willingness on the part of the patent owner to enforce its patent, an ANDA applicant had no reasonable apprehension of suit and, consequently, could not bring a declaratory judgment action.[113]

In January 2007, the Supreme Court addressed declaratory judgment standards in *MedImmune, Inc. v. Genentech, Inc.*[114] This case involved an appeal by a patent licensee, who was seeking "a declaratory judgment that the underlying patent [was] invalid, unenforceable, or not infringed" while it continued to pay royalties to the patent licensor. The Supreme Court held that Article III of the Constitution does not require a patent licensee to breach its license agreement in order to file a declaratory judgment action regarding noninfringement, invalidity, or unenforceability.[115] In arriving at its decision, the Court reaffirmed that a plaintiff seeking a declaratory judgment must satisfy Article III's case or controversy requirement,[116] and, in a footnote, it criticized the reasonable apprehension of suit test developed

[109] See, for example, the ticlopidine matter discussed in section II. B. 2. a. and the pravastatin matter discussed in section II. B. 2. b.

[110] The failure to market forfeiture provision provides that a declaratory judgment of invalidity or noninfringement from which no appeal has been or can be taken will satisfy the second prong of this provision. 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(AA).

[111] The Federal Circuit has exclusive jurisdiction over appeals of district court decisions relating to civil actions arising under any federal law relating to patents. 28 U.S.C. § 1295(a)(1) ("The United States Court of Appeals for the Federal Circuit shall have exclusive jurisdiction ... of an appeal from a final decision of a district court of the United States ... if the jurisdiction of that court was based, in whole or in part, on section 1338 of [title 35 of the U.S. Code] ... ."). Section 1338 provides that "[t]he district courts shall have original jurisdiction of any civil action arising under any Act of Congress relating to patents. ..." 21 U.S.C. § 1338(a).

[112] Teva Pharms. USA, Inc. v. Novartis Pharms. Corp., 482 F.3d 1330, 1339 (Fed. Cir. 2007), *rehear'g denied and rehear'g en banc denied*, No. 06-1181, 2007 U.S. App. LEXIS 16048 (Fed. Cir. June 20, 2007). The requirement for a reasonable apprehension of suit was part of a two-prong test formulated by the Federal Circuit to determine if an actual controversy existed in declaratory judgment actions. The other prong required present activity which could constitute infringement or concrete steps taken with the intent to conduct such activity. *Id.*

[113] *See, e.g.*, Dr. Reddy's Labs., Ltd. v. Pfizer Inc., No. 03-cv-726, 2003 U.S. Dist. LEXIS 24351, at 14-15 (D. N.J. July 8, 2003) ("The objective actions of the patentee must rise 'to a level sufficient to indicate an intent to enforce its patent', i.e., to initiate an infringement action.") (citation omitted) (unpublished).

[114] 549 U.S. 118 (2007).

[115] *Id.* at 137.

[116] *Id.* at 126-27.

by the Federal Circuit.[117] The Supreme Court instead directed courts to determine "whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment."[118]

Subsequent to the *MedImmune* decision, the Federal Circuit put aside the reasonable apprehension of suit test for cases seeking declaratory judgment to trigger 180-day exclusivity or forfeiture, concluding that *MedImmune* requires instead an all-of-the-circumstances test.[119] Five cases have been decided by the Federal Circuit under the new standard, to date, and in two of the five the declaratory judgment suit was permitted to proceed.[120] The other three cases were dismissed for lack of jurisdiction.[121] The outcome of these cases appears to be very fact-specific, as one would expect from an all-the-circumstances test. At this point, it does not seem possible to draw out general rules or list a series of factors that indisputably would, or would not, give rise to jurisdiction. That said, it is clear that there have been circumstances in which courts have found federal court jurisdiction even where the NDA holder has provided a covenant not to sue the generic applicant seeking relief. It is therefore possible that more generic applicants will seek declaratory judgments of patent invalidity or noninfringement when the patent owner or NDA holder does not sue the applicant on at least one of the challenged patents.[122]

C. *Commercial Marketing Trigger*

1. *Will marketing by the first applicant of the innovator's product under a private generic label satisfy the commercial marketing trigger?*

Any commercial marketing by the first generic applicant, including commercial marketing of an "authorized generic," discussed below in section IV. B. 1., will trig-

[117] *Id.* at 132 n.11.

[118] *Id.* at 127.

[119] Teva Pharms. USA, Inc. v. Novartis Pharms. Corp., 482 F.3d 1330, 1339 (Fed. Cir. 2007). Teva filed an ANDA with paragraph IV certifications for all five of the listed patents. Novartis, the NDA holder, sued for patent infringement on one of five patents. Teva then brought a declaratory judgment action on the four other patents. The district court, which issued its decision prior to *MedImmune*, dismissed the action for lack of subject matter jurisdiction after finding no reasonable apprehension of suit. On appeal, the Federal Circuit acknowledged that the Supreme Court had "overruled" the reasonable apprehension of suit test in MedImmune and thus applied an "all-of-the-circumstances" test. *Id.* at 1338 ("Thus, because the Supreme Court in *MedImmune* cautioned that our declaratory judgment 'reasonable-apprehension-of-suit' test 'contradict[s]' and 'conflicts' with its precedent, these Federal Circuit tests have been 'overruled by ... an intervening ... Supreme Court decision.'") (citations omitted).

[120] Teva Pharms. USA, Inc. v. Novartis Pharms. Corp., 482 F.3d 1330 (Fed. Cir. 2007); Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc., 527 F.3d 1278 (Fed. Cir. 2008), *petition for rehear'g and rehear'g en banc denied*, No. 2007-1404, 2008 U.S. App. LEXIS 15741 (Fed. Cir. June 24, 2008) *cert. denied*, No. 08-624, 2009 U.S. LEXIS 1482 (Feb. 23, 2009).

[121] Merck & Co., Inc. v. Apotex, Inc., No. 2007-1362, 2008 U.S. App. LEXIS 15014, (Fed. Cir. July 16, 2008) (unpublished); Merck & Co., Inc. v. Apotex, Inc., 292 Fed. Appx. 38 (Fed. Cir. Aug. 21, 2008); Janssen Pharmaceutica, N.V. v. Apotex, Inc., 540 F.3d 1353 (Fed. Cir. 2008), *rehear'g denied and rehear'g en banc denied*, No. 2008-1062, 2008 U.S. App. LEXIS 25387 (Fed. Cir. Oct. 29, 2008), *cert. denied*, No. 08-959, 2009 U.S. LEXIS 2021 (2009).

[122] One bill introduced in the 110th Congress regarding settlements between innovators and generic companies would have made dismissal of an ANDA applicant's declaratory judgment action of noninfringement or invalidity for lack of subject matter jurisdiction a forfeiture event. H.R. 1902, 110th Cong. (2007). This bill would also have made the grant of a covenant not to sue a forfeiture event if the generic manufacturer filed the covenant with FDA. A hearing was held by the Subcommittee on Commerce, Trade and Consumer Protection of the House Committee on Energy and Commerce on the measure, and it was subsequently referred to the Subcommittee on Courts, the Internet, and Intellectual Property of the House Judiciary Committee. The bill was never reported out of committee. Similar legislation has been introduced in the 111th Congress, and a hearing by the Subcommittee on Commerce, Trade, and Consumer Protection of the House Committee on Energy and Commerce on the bill was held on Mar. 31, 2009. H.R. 1706, 111th Cong. (2009).

ger exclusivity, whether the application is an old ANDA or a new ANDA. There have been no developments with respect to this issue since the authors last wrote.

For old ANDAs, the issue was addressed in 2001 by a district court in West Virginia. In April 1997, Mylan had submitted an ANDA with a paragraph IV certification to the 30 mg dosage of extended release nifedipine and was, therefore, considered the first applicant. The innovator, Pfizer, sued Mylan, for infringement, and the parties settled in February 2000. Although the settlement terms were not made public or given to the court, the court stated that Pfizer apparently licensed Mylan to sell a private label version of its own 30 mg, 60 mg, and 90 mg nifedipine extended release products. Pfizer may also have permitted Mylan to market its own 30 mg product under its own ANDA, but Mylan never did so. Mylan claimed the settlement allowed it to maintain its paragraph IV certification, and it never amended the paragraph IV certification to a paragraph III certification.

After the settlement, Biovail, a generic manufacturer aspiring to market nifedipine, attempted without success to persuade Mylan to waive its 180-day exclusivity. When this failed, Teva (Biovail's licensee) submitted a citizen petition to FDA asking the agency to find either: a) the Mylan ANDA was not eligible for exclusivity, or b) any exclusivity had expired. FDA responded in February 2001, agreeing on both grounds. The agency reasoned, first, that the settlement effectively turned Mylan's paragraph IV certification into a paragraph III certification, and second, that the private label sales constituted commercial marketing and triggered exclusivity. Because the 180 days had expired, FDA approved Biovail's ANDA. Mylan brought suit.

In the decision that resulted, the district court found that FDA had been unreasonable on the first issue and reasonable on the second. The court was not prepared to allow FDA unilaterally to deem the paragraph IV certification to be a paragraph III certification, particularly since Mylan had not amended the certification in its ANDA. But it upheld FDA's determination that the private label sales were commercial marketing, and thus the 180-day period had expired. In short, the district court held that a generic manufacturer begins commercial marketing, and thereby starts the 180-day clock, even when it sells a private label version of the innovator's product, rather than the product that is the subject of its ANDA.[123]

For new ANDAs, Congress provided in 2003 that if an ANDA contains a paragraph IV certification and "is for a drug for which a first applicant has submitted an application containing such a certification" (i.e., is for a drug for which someone else submitted an ANDA earning it exclusivity) the application "shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant."[124]

2. *Does 180-day exclusivity, if triggered by commercial marketing prior to a final, unappealable decision of the court, continue to run during the pendency of a preliminary injunction prohibiting further commercial marketing by the first applicant?*

If 180-day exclusivity is triggered by commercial marketing prior to a final, unappealable decision of the court, and the innovator subsequently obtains a preliminary

[123] Mylan Pharms., Inc. v. Thompson, 207 F. Supp. 2d 476 (N.D. W.Va. 2001).

[124] 21 U.S.C. § 355(j)(5)(B)(iv)(I).

injunction prohibiting further commercial marketing by the first applicant, the new legislative language suggests that the first applicant's exclusivity continues to run, even though it cannot market its product. This is also presumably the case for old ANDAs. Although a case involving an old ANDA was brought, it was dismissed without a decission in the wake of a ruling upholding the validity of the patent at issue in a separate infringement action. The authors begin with the case involving the old ANDA.

Apotex filed the first ANDA to market a generic version of Plavix (clopidogrel bisulfate). The ANDA included a paragraph IV certification challenging the validity of one of two listed patents for Plavix. Sanofi-Synthelabo, the maker of Plavix, sued Apotex for patent infringement in a district court in New York.[125] The 30-month stay triggered by the lawsuit expired, and FDA approved Apotex's ANDA on January 20, 2006. Apotex began to commercially market its product on August 8, 2006, thus triggering its 180-day exclusivity. On August 31, the district court preliminarily enjoined Apotex from selling clopidogrel bisulfate pending a final decision on the merits.[126] After a bench trial in early 2007, the district court upheld the validity of the patent in question and entered a permanent injunction against further infringement of the patent by Apotex.[127] At the end of 2008, the Federal Circuit affirmed the New York district court's finding of validity with respect to the patent at issue.[128] Apotex's petition for panel rehearing and rehearing en banc was denied on March 26, 2009.

In the meantime, several generic manufacturers submitted ANDAs with paragraph IV certifications, and Sanofi sued each. FDA gave final approval to Dr. Reddy's ANDA on January 14, 2008. Patent litigation is still pending against Dr. Reddy's,[129] however, and apparently the company has not begun to market its approved product. Apotex, which had begun its 180-day exclusivity and, as noted, is now enjoined from further marketing, petitioned the agency to stay the effective date of final approval of Dr. Reddy's ANDA (and any other pending ANDA for clopidogrel bisulfate with a paragraph IV certification for the patent in question) until the earlier of: a) 156 days after the injunction barring Apotex from marketing clopidogrel bisulfate was lifted or b) expiry of the patent at issue.[130]

In essence, Apotex argued that the statute governing old ANDAs does not require FDA to approve a subsequent application on the 181st day after commercial marketing begins. Instead, a subsequent applicant's ANDA "shall be made effective *not earlier than* one hundred eighty days after" the date the Secretary receives notice from the first filer of commercial marketing.[131] This, Apotex argued, gives FDA discretion to delay the effective date of approval of ANDAs submitted by subsequent filers. Apotex further contended that by granting it the balance of its

[125] Sanofi-Synthelabo v. Apotex, Inc., No. 02-cv-2255 (S.D.N.Y. Mar. 21, 2002).

[126] Sanofi-Synthelabo v. Apotex, Inc., 488 F. Supp. 2d 317, 350 (S.D.N.Y. 2006), *aff'd*, 470 F.3d 1368, 1372 (Fed. Cir. 2006), *rehear'g and rehear'g en banc denied*, No. 2006-1613, 2007 U.S. App. LEXIS 2807 (Fed. Cir. Jan. 19, 2007).

[127] Sanofi-Synthelabo v. Apotex, Inc., 492 F. Supp. 2d 353, 356, 397-98 (S.D.N.Y. 2007).

[128] Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075 (Fed. Cir. 2008).

[129] On January 24, 2008, Dr. Reddy's and Sanofi stipulated that Dr. Reddy's will provide Sanofi with at least 10 business days notice before it begins to manufacture, use, offer to sell, or sell within the United States or import into the United States any product claiming the patent at issue. If the Federal Circuit enters a final judgment holding claim #3 of the patent at issue invalid, however, Dr. Reddy's will not be required to give notice. Sanofi-Synthelabo v. Dr. Reddy's Labs., Ltd., No. 02-cv-3672 (S.D.N.Y. Jan. 24, 2008) (stipulation and order).

[130] Apotex, Inc., Petition for Stay of Action, Docket No. FDA-2008-P-0117 (Feb. 13, 2008) (pending).

[131] *See* 21 U.S.C. § 355(j)(5)(B)(iv) (1984) (amended 2003)(emphasis added).

180-day exclusivity if it succeeded on its patent challenge, FDA would best serve Congress's intent to promote competition in the drug marketplace and create meaningful economic incentives to encourage patent challenges. Apotex followed this petition with a lawsuit against FDA seeking declaratory and injunctive relief.[132] FDA successfully moved for an extension of time to answer Apotex's complaint on four occasions, citing the Federal Circuit's decision on the underlying patent litigation. Because Apotex's petition for panel rehearing and rehearing en banc was denied, it has lost its patent challenge and its eligibility for 180-day exclusivity is no longer at issue.[133] As a result, Apotex's lawsuit against FDA was voluntarily dismissed on April 15, 2009.[134] In addition, Apotex's petition, which remains unanswered, should be considered moot.

For new ANDAs, the exclusivity period is calculated from the date of the first commercial marketing of the drug product by a first applicant. The provision on which Apotex relied in its case, however, was amended by Congress. Section 505(j)(5)(B)(iv) now states that a subsequent application "shall be made effective *on the date that is 180 days after the date of the first commercial marketing*" of the first generic product.[135] Whatever the merits of Apotex's argument regarding old ANDAs, its reasoning appears to be inapplicable to new ANDAs. It seems that once triggered, exclusivity runs, even if the holder of the exclusivity is enjoined from marketing its product.

3. *Do 180-day exclusivity and pediatric exclusivity run concurrently or consecutively?*

The relationship between 180-day exclusivity and pediatric exclusivity was an issue for old ANDAs, because the court decision trigger and the agency's patent-by-patent approach to exclusivity meant that a first generic's exclusivity could be triggered by a court decision during the innovator's pediatric exclusivity term. As noted in the 2007 article, the issue arose in the context of a situation in which there were different rulings on two patents, with one patent being upheld, to which the pediatric exclusivity would be applied. Although FDA requested comment on the issue in 2001[136] and seemed poised to find that the terms overlapped,[137] the issue was never addressed by a court. Congress confirmed in the Best Pharmaceuticals for Children Act (BPCA) that if an innovator earns six months of pediatric exclusivity, the first generic applicant's ANDA is approved effective the first day after conclusion of that exclusivity, and the 180 days begin to run at that point. The terms are consecutive.[138]

As noted above, 180-day exclusivity for new ANDAs is awarded on a product-by-product basis, and there is no court decision trigger for exclusivity. Accordingly, the statutory structure may eliminate the ability of a subsequent filer to trigger a first filer's exclusivity during the innovator's pediatric exclusivity term. There is, however, a court decision trigger for forfeiture and, accordingly, a new question

[132] Apotex Inc. v. Leavitt, No. 08-cv-00693 (D.D.C. Apr. 23, 2008) (complaint).

[133] *See* 21 C.F.R. § 314.94(a)(12)(viii)(A).

[134] Apotex Inc. v. Johnson, No. 08-cv-00693 (D.D.C. Apr. 15, 2009)(notice of voluntary dismissal without prejudice).

[135] 21 U.S.C. § 355(j)(5)(B)(iv)(I) (emphasis added).

[136] 66 Fed. Reg. 27,983 (May 21, 2001).

[137] *See* the discussion in 2007 of Eli Lilly & Co. v. Barr Laboratories, Inc., 222 F.3d 973 (Fed. Cir. 2000).

[138] Pub. L. No. 107-109, 115 Stat. 1408 (2002). Section 505A(k) of the FDCA, now section 505A(m), states that if the 180-day exclusivity period "overlaps" with a 6-month pediatric exclusivity period, such that the first generic applicant loses a portion of the 180-day period to which it is entitled, the 180-day period is extended by the number of days of overlap.

whether the failure to market clock is tolled during pediatric exclusivity. At the end of 2008, a district court in the District of Columbia rejected the argument that the forfeiture clock is tolled. The case is discussed in more detail below (see section III. A. 3. b. ii.), but the relevant facts are as follows.

Hi-Tech Pharmacal Co. was the first applicant to submit a substantially complete ANDA for a generic version of Cosopt (dorzolamide hydrochloride/timolol maleate). One of the listed patents expired on April 28, 2008, but had a period of pediatric exclusivity until October 28, 2008. The other listed patents were due to expire later. Hi-Tech submitted paragraph IV certifications for all listed patents, but the NDA holder, Merck, sued only for infringement of the patent set to expire on April 28, 2008. It disclaimed the other patents and asked that they be delisted. Merck prevailed in its patent case, and Hi-Tech was enjoined from selling generic Cosopt products. The court also ordered that the effective date of approval of the Hi-Tech ANDA be no earlier than October 28, 2008.

Forfeiture became an issue because one patent expired in April 2008 (although subject to pediatric exclusivity), and two patents were to be delisted. Among other things, Hi-Tech argued that it had no legal right to market prior to expiration of pediatric exclusivity, so it could not be deemed to have forfeited on the basis of failure to market. In other words, it argued that under the BPCA, the forfeiture clock is tolled during the pediatric exclusivity term. The court rejected this argument, noting that under the BPCA, tolling occurs only if pediatric exclusivity "overlaps" with the 180-day exclusivity period. The court agreed with FDA that there was no overlap in Hi-Tech's case because under the post-MMA provisions (i.e. product-by-product exclusivity and no court decision trigger), pediatric exclusivity and 180-day exclusivity cannot overlap.[139]

III. LOSS OF ELIGIBILITY AND FORFEITURE

A. *General Rules*

1. *How does the court decision forfeiture trigger work?*

The court decision trigger for forfeiture states that 180-day exclusivity is forfeited if the applicant fails to market 75 days after, as to each patent at issue, "a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed"—unless 75 days have not elapsed since the ANDA approval was effective *and* 30 months have not elapsed since the ANDA was submitted. Put another way, forfeiture occurs if: 1) every patent as to which the first applicant filed a paragraph IV certification has been declared invalid or not infringed in a final court decision, and 75 days have elapsed since the last such decision; *and* 2) 30 months have elapsed since the ANDA was submitted *or* FDA has granted final approval to the ANDA, and 75 days have elapsed since that approval was effective.

There have been no petitions or, to the authors' knowledge, court cases involving interpretation of this forfeiture provision, and they think that agency interpretations of the court decision trigger for exclusivity may apply. Thus, for example, the agency may interpret the court decision trigger for forfeiture to require "a decision of a court that on its face evidences a holding on the merits of patent noninfringement,

[139] Hi-Tech Pharmacal Co., Inc. v. FDA, 587 F. Supp. 2d 13, 21-22 (D.D.C. 2008).

invalidity, or unenforceability."[140] This would be consistent with the position it announced in the pravastatin matter regarding court decisions triggering exclusivity (see section II. B. 2. b.)

2. *What is the effect of patent expiry once a paragraph IV certification has been submitted?*

When the authors last wrote, it was clear that if a patent expires before the first generic applicant has final approval of its ANDA, the applicant must amend its certification from a paragraph IV to a paragraph II and will no longer be entitled to 180-day exclusivity when its ANDA is finally approved. It is now also clear that it is FDA's policy that if the patent expires after the first generic applicant has final approval of its ANDA but before the 180-day exclusivity period has ended, the applicant is no longer entitled to exclusivity as of the date of the patent's expiration.

a. *Patent expiry before final approval.*

Andrx was the first to file a paragraph IV certification with respect to 10 of the 11 patents listed by AstraZeneca in relation to the 40 mg version of its product Prilosec (omeprazole). Dr. Reddy's was the first to file a paragraph IV certification for the 40 mg version on the other patent. (Andrx had filed a paragraph III.) The patent expired after both ANDAs were tentatively approved, but before either was finally approved. FDA concluded that Dr. Reddy's lost its eligibility for exclusivity when the patent expired, on the theory that the company was required at that time to amend its ANDA to convert the paragraph IV certification to a paragraph II certification.[141] Dr. Reddy's brought suit against FDA, arguing that the agency may not require a generic applicant to amend its certification prior to final ANDA approval, and that an ANDA is eligible for exclusivity if it contains the appropriate paragraph IV certification at the time of filing. The district court found the statute ambiguous on both points, however, and upheld the agency's decision.[142] Thus Dr. Reddy's was not entitled to share Andrx's 180-day exclusivity.

b. *Patent expiry before conclusion of 180-day exclusivity.*

Mylan submitted the first ANDA to market generic versions of 2.5 mg, 5 mg, and 10 mg Norvasc (amlodipine besylate) tablets on May 22, 2002. The ANDA contained paragraph IV certifications for the two patents Pfizer had listed for the drug. The later of these two patents, and the one at issue, was due to expire on March 25, 2007. The other patent was due to expire on July 31, 2006. Pfizer sued Mylan for patent infringement, but it did not file its lawsuit within 45 days of receiving notice of Mylan's paragraph IV certification. As a result, no 30-month stay of approval applied. On October 3, 2005, FDA approved Mylan's ANDA. In

[140] *See* Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Pravastatin ANDA Applicant 15 (Apr. 11, 2006), *available at* www.fda.gov/cder/ogd/announce/Pravastatin-180Day-amend.pdf.

[141] *See* 21 C.F.R. § 314.94(a)(12)(viii)(C).

[142] Dr. Reddy's Labs., Inc. v. Thompson, 302 F. Supp. 2d 340 (D.N.J. (2003)). The court also noted that the agency had set forth its interpretation of the statute at least twice prior to its decision on Dr. Reddy's application. *Id.* at 351, *citing* 59 Fed. Reg. 50,338, 50,348 (Oct. 3, 1994) ("a patent is deemed to be relevant until the end of the term of the patent or applicable 180-day period, whichever occurs first") *and* FDA, Response to APP and Pharmachemie Citizen Petitions, Docket No. 1999P-1271 (Aug. 2, 1999). The court characterized the latter as stating that "because exclusivity cannot extend beyond the expiration of a patent, an ANDA applicant who is first to file a paragraph IV certification on a patent loses its eligibility based upon that patent when the patent expires before either of the triggering events occurs."

February 2007, a district court in Pennsylvania held that Mylan infringed Pfizer's remaining unexpired patent (the one due to expire in 2007).[143] On March 16, 2007, the district court enjoined Mylan from marketing its generic product and ordered that the effective date of any approval of Mylan's ANDA be no earlier than patent expiry.[144]

Mylan appealed and sought a stay of the district court's order.[145] The Federal Circuit granted the stay on March 23, 2007, and Mylan launched its generic amlodipine product that same day.[146] On March 25, 2007, the patent expired. The following day, Mylan submitted a Petition for Stay of Action to FDA requesting that the agency not issue final approval to any ANDAs for generic amlodipine tablets until Mylan's 180-day exclusivity expired on September 23, 2007.[147] Mylan also sued FDA claiming it was entitled to 180-day exclusivity and requesting that the court enjoin FDA from approving other ANDAs for amlodipine until the merits of its claim could be heard. FDA proposed to seek comments from interested parties before it responded. The district court ordered FDA to provide a decision by April 11, 2007, and to take no action on pending ANDAs for amlodipine until April 13, 2007.[148]

The agency opened a docket and solicited comments on, among others, the question whether "180-day exclusivity triggered before a patent expires continue[s] to bar approvals of other ANDAs after the patent expires, even if other ANDA applicants change their certifications to paragraph II or withdraw their certifications altogether?"[149] While many of those submitting comments to FDA argued that the agency had a longstanding position that 180-day exclusivity does not extend beyond patent expiration, Mylan asserted that once the period of 180-day exclusivity is triggered, the first applicant's right to exclusivity is vested and consequently cannot be forfeited. The agency concluded, however, that Mylan's exclusivity terminated when the patent expired on March 25, 2007. It noted that both the statute and its own regulations require ANDA applicants to change their paragraph IV certifications to paragraph II certifications when a patent expires.[150] Applications with paragraph II certifications are eligible for immediate approval upon patent expiry.[151] Therefore, because paragraph IV certifications cease to be accurate upon patent expiry, once a patent expires, neither the patent nor the 180-day exclusivity based

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[143] Pfizer, Inc. v. Mylan Labs., Inc., No. 02-cv-1628, 2007 U.S. Dist. LEXIS 14417 (W.D. Pa. Feb. 27, 2007).

[144] Pfizer, Inc. v. Mylan Labs., Inc., No. 02-cv-1628, 2007 U.S. Dist. LEXIS 18699 (W.D. Pa. Mar. 16, 2007), *rev'd*, 236 Fed. Appx. 608 (Fed. Cir. 2007) (unpublished).

[145] In the meantime, in a case involving another ANDA applicant, the Federal Circuit held invalid three claims in the patent. Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348 (Fed. Cir. (2007)), *cert. denied*, 128 S. Ct. 110 (2007).

[146] Because the Federal Circuit stayed the district court order, FDA determined that it had "no basis to convert the approval status of Mylan's ANDA from approved to tentatively approved." Letter from Gary J. Buehler, Director, FDA Office of Generic Drugs, to ANDA Applicant/Holder for Amlodipine Besylate Tablets 5 n.4 (Apr. 18, 2007).

[147] Mylan Pharmaceuticals, Petition for Stay of Action, Docket No. 2007P-0116 (Mar. 26, 2007).

[148] Mylan Labs., Inc. v. Leavitt, No. 07-cv-579 (D.D.C. Mar. 26, 2007) (order). These deadlines were extended to April 18 and April 20, respectively. Mylan Labs., Inc. v. Leavitt, No. 07-cv-579 (D.D.C. Apr. 10, 2007) (order).

[149] FDA, Request for Comments: Amlodipine ANDA Approvals, Docket No. 2007N-0123 (Mar. 28, 2007).

[150] *See* 21 U.S.C. § 355(j)(2)(A)(vii)(II); 21 C.F.R. § 314.94(a)(12)(viii)(C) ("[A]n applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate").

[151] *See* 21 U.S.C. § 355(j)(5)(B)(i) (stating that when an applicant files a paragraph II certification, approval of the applicant's ANDA "may be made effective immediately"); 21 C.F.R. § 314.94(a)(12)(viii).

on a paragraph IV certification to that patent presents a barrier to the approval of subsequent ANDAs. The court found FDA's decision "reasonable."[152]

It would be consistent for FDA to reach the same conclusion with respect to new ANDAs, although of course exclusivity is earned on a product-by-product basis, rather than a patent-by-patent basis. Applied to new ANDAs, this conclusion suggests that if all of the patents as to which the first applicant filed a paragraph IV certification qualifying it for exclusivity expire before the first generic applicant has final approval of its ANDA, the applicant must amend its certifications from paragraph IV to paragraph II and will no longer be entitled to 180 days of exclusivity when its ANDA is finally approved. Moreover, if all of these patents expire after the first generic applicant has final approval of its ANDA but before the 180-day exclusivity period has ended, presumably the applicant is no longer entitled to exclusivity. Indeed, the 2003 legislation states clearly that the first applicant forfeits exclusivity if all of the patents as to which it filed a paragraph IV certification qualifying it for exclusivity have expired.[153] It does not differentiate between expiry before final approval and expiry after final approval.

3. *What is the effect of delisting a patent once a paragraph IV certification has been submitted?*

a. *Old ANDAs.*

As noted in the authors' 2007 article, with respect to old ANDAs, generally speaking, if a patent is removed from the *Orange Book*, FDA requires ANDA applicants to delete their paragraph IV certifications. FDA's policy creating an exception if a first ANDA applicant was sued by the patent owner was found to be inconsistent with the statute. The case in question, involving generic simvastatin and usually referred to as the *Ranbaxy* case, was discussed in the authors' last article. It is discussed again below, because it continues to be relevant. There has been one case since the last article. This case, involving generic risperidone, confirms that if a patent is removed from the electronic *Orange Book* prior to submission of the ANDA in question, a paragraph IV certification is inappropriate even if the paper *Orange Book* has not been revised.

i. *The Ranbaxy case.*

IVAX sought approval of 5 mg, 10 mg, 20 mg, and 40 mg generic versions of Merck's Zocor (simvastatin). IVAX was the first generic applicant to challenge two patents claiming approved methods of use. The patents in question apparently claimed compounds related to simvastatin, rather than simvastatin itself.[154] Following submission of the IVAX ANDA, FDA amended its regulations to state that listed drug substance patents must claim the active ingredient of an approved drug product, rather than a metabolite or an intermediate.[155] At Merck's request,

[152] Mylan Labs. Inc. v. Leavitt, 484 F. Supp. 2d 109, 122-23 (D.D.C. 2007). The appeal was later dismissed as moot. Mylan Labs. Inc. v. Leavitt, No. 07-5156, 2007 U.S. App. LEXIS 24964 (D.C. Cir. Oct. 23, 2007).

[153] 21 U.S.C. § 355(j)(5)(D)(i)(VI).

[154] The FTC characterized the substance as "related to" simvastatin. FTC, Response to Citizen Petition by IVAX Pharmaceuticals, Inc., Docket No. 2005P-0008 (Apr. 5, 2005), at 4. Ranbaxy characterized the compounds as "related compounds of simvastatin" that it believed to be "present in Zocor" and that were "a byproduct of Merck's manufacture of simvastatin." Ranbaxy Laboratories Limited, Citizen Petition, Docket No. 2005P-0046 (Feb. 1, 2005), at 2.

[155] 68 Fed. Reg. 36,676 (June 18, 2003).

and following several additional letters to the Agency (from private law firms, presumably representing generic company interests) stating that the patents should not be listed, the agency removed the patents from the *Orange Book*. This had the effect of permitting subsequent ANDA applicants to omit certifications relating to the patents. IVAX petitioned the agency to relist the patents and not approve subsequent ANDAs until its exclusivity had concluded.[156] Ranbaxy filed a citizen petition with respect to 80 mg simvastatin and raised the same issue with respect to the same two delisted patents.[157] Teva opposed the petitions, arguing that "incorrectly listed patents cannot support exclusivity."[158]

FDA denied both petitions, stating that it does "not interpret the statute to require that an ANDA applicant who has submitted the first paragraph IV certification to a patent always remain eligible for 180-day exclusivity as to that patent even if the NDA holder has asked that the patent be delisted."[159] Instead, FDA noted, it is "consistent with the language and purposes of the statute generally to delist a patent when the NDA holder requests that we do so" and to therefore "remove the basis for exclusivity as to that patent." There is "one limited exception" in the regulations, pursuant to which FDA maintains the listing of a patent where the paragraph IV challenge of the first ANDA applicant has resulted in litigation. This ensures that victory in the patent litigation, which would result in delisting of the patent, will not also result in loss of exclusivity. Merck had not sued either IVAX or Ranbaxy, however, so this limited exception did not apply. The patents were delisted, and FDA concluded that neither generic manufacturer was entitled to exclusivity with respect to the patents.

In litigation that followed, however, both the district court and the D.C. Circuit found that FDA should *not* have delisted the patents. The district court noted that section 505(j)(5)(B)(iv) is "clear and unambiguous" in providing that the first generic applicant may qualify for exclusivity "in one of two ways"—a court decision or commercial marketing. Further, "[o]f the two methods Congress has provided by which the first ANDA applicant's 180-day period of exclusivity is triggered, one requires litigation and one does not." The issue, according to the court, was whether FDA could "effectively restrict the reward to only a sued ANDA holder, by delisting a patent after the ANDA holder successfully avoided suit." It noted that the "delisting practice as applied here effectively eliminated Congress's 'first commercial marketing' trigger, in violation of the clear command of Congress." Although FDA may adopt a delisting practice, it cannot favor "one of two equal statutory provisions over the other."[160] The agency relisted the patents in June 2006, and in November the Court of Appeals affirmed the lower court's decision.[161]

ii. *The risperidone case.*

On August 3, 2007, Teva submitted a citizen petition to FDA stating that it was the first ANDA applicant to submit a paragraph IV certification for one of two patents listed for 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg Risperdal (risperidone) tablets and thus should be eligible for exclusivity.[162] The patent referenced in Teva's

[156] IVAX Pharmaceuticals, Inc., Citizen Petition, Docket No. 2005P-0008 (Jan. 5, 2005).

[157] Ranbaxy Laboratories Limited, Citizen Petition, Docket No. 2005P-0046 (Feb. 1, 2005).

[158] Teva, Response, Docket No. 2005P-0046 (June 8, 2005), at 2.

[159] FDA, Response, Docket Nos. 2005P-0008 and 2005P-0046 (Oct. 24, 2005).

[160] Ranbaxy Labs., Ltd. v. Leavitt, 459 F. Supp. 2d 1 (D.D.C. 2006).

[161] Ranbaxy Labs., Ltd. v. Leavitt, 469 F.3d 120 (D.C. Cir. 2006).

[162] Teva Pharmaceuticals USA, Inc., Citizen Petition, Docket No. 2007P-0316 (Docket No. FDA-2007-P-0170) (Aug. 3, 2007).

paragraph IV certification, the '952 patent, was listed as expiring on October 27, 2009. Teva submitted a paragraph III certification with respect to the other patent, which had a period of pediatric exclusivity scheduled to end on June 29, 2008.

Teva contended that the '952 patent appeared in the "official" or printed edition of the *Orange Book* on August 28, 2001, the date on which Teva submitted its ANDA and paragraph IV certification. According to Teva, FDA notified the company on October 12, 2001, that the agency had delisted the patent from the *Orange Book* at the request of Johnson & Johnson (J&J) (Janssen, the manufacturer of Risperdal, is part of the J&J family of companies) and refused to file its ANDA unless Teva modified its patent certification to reflect that the patent was no longer listed. Teva argued that the "official" delisting of the patent did not occur until January 2002 when FDA issued a revised printed edition of the *Orange Book* and that the agency should relist the patent and confirm Teva's right to 180-day exclusivity. Teva cited *Ranbaxy*, arguing that FDA may not delist a patent after a company submits an ANDA with a paragraph IV certification to that patent.

FDA denied Teva's request to relist the patent.[163] The agency had modified its patent listing database on June 11, 2001, prior to submission of Teva's ANDA, to remove the patent in question from the entries for Risperdal tablets. Moreover, when Teva submitted its ANDA, the electronic *Orange Book* contained the most current information regarding patents listed for Risperdal tablets and, in particular, did not include the patent in question. According to FDA, Teva's "assertion that the delisting of the '952 patent did not become effective until publication of the 2002 annual edition of the Orange Book" was "without merit." Accordingly, FDA ruled that because the delisting was proper, Teva was not eligible for 180-day exclusivity.

In litigation that followed, the district court granted summary judgment to Teva and required FDA to relist the patent in the *Orange Book* and restore Teva's paragraph IV certification and 180-day exclusivity.[164] The court of appeals reversed,[165] explaining that the FDCA provides that a "successful paragraph IV certification must identify a patent that 'claims the listed drug' or that 'claims a use for such listed drug for which the applicant is seeking approval.'" If there is no patent that claims the listed drug, "there can be no valid certification" and thus no 180-day exclusivity. Moreover, "[a]ll patent claim information is provided by the NDA holder." Thus, "as a practical matter, a patent claims a drug when the NDA holder says it does." In this case, when Teva submitted its ANDA for generic Risperdal, Janssen had already notified FDA that it had withdrawn the patent. In addition, FDA had removed the listing from the electronic version of the *Orange Book* and thus informed Teva of its action. The D.C. Circuit found that although the printed version of the *Orange Book* still listed the patent, "[i]nadvertent failure by the agency to meet its separate publication requirement cannot defeat facts."

b. *New ANDAs.*

For new ANDAs, the MMA contains a forfeiture provision based on withdrawal of patent listings. Specifically, if 75 days have elapsed since approval of the first applicant's ANDA was made effective (or 30 months have elapsed since the first applicant's ANDA was submitted), then if the last of the patents qualifying it for exclusivity is delisted, the first applicant will forfeit exclusivity if it fails to market

[163] FDA, Response, Docket No. 2007P-0316 (Docket No. FDA-2007-P-0170) (Feb. 26, 2008).

[164] Teva Pharms. USA, Inc. v. Leavitt, No. 08-cv-00395 (D.D.C. April 11, 2008) (order).

[165] Teva Pharms., USA, Inc. v. Leavitt, No. 08-5141, 2008 U.S. App. LEXIS 23638 (D.C. Cir. Sept. 12, 2008), *judgment entered by*, 548 F.3d 103 (D.C. Cir. 2008).

within 75 days.[166] The agency has now twice invoked the withdrawal of patent listings to find forfeiture.

i. *Generic acarbose.*

On March 22, 2005, Cobalt became the first applicant to submit an ANDA for a generic version of Precose (acarbose) tablets. The ANDA contained a paragraph IV certification for the one patent listed for Precose tablets. Bayer, the NDA holder, did not file a patent infringement action against Cobalt. In a letter dated September 26, 2007, to applicants with pending ANDAs for generic acarbose tablets, FDA stated that more than 30 months had passed since it had received the first applicant's ANDA. It also noted that Bayer had requested that the agency delist the patent in question.[167] The agency asked for comments regarding the applicability of several forfeiture provisions to the first applicant's eligibility for 180-day exclusivity, including the delisting forfeiture event under the failure to market provision.[168]

In a letter dated May 7, 2008, FDA approved Cobalt's ANDA but concluded that the company had forfeited its 180-day exclusivity because it did not begin to market its product by September 22, 2007. For purposes of the first prong of the failure to market provision, FDA concluded that September 22, 2007, was the "earlier of" — 1) the date that was 30 months from the date on which Cobalt submitted a substantially complete ANDA containing a paragraph IV certification to the patent[169] and 2) the date that was 75 days after FDA approved Cobalt's ANDA.[170] FDA also concluded that the triggering event for the second prong of the failure to market provision was Bayer's request to delist the Precose patent on April 16, 2007.[171] Based on this finding,[172]

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[166] 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC).

[167] The agency has adopted a new policy of not delisting patents from the *Orange Book* upon request by the innovator. Instead it waits until 75 days have passed and a forfeiture decision is required. As explained by the agency, "[b]ecause immediate removal of patent information from the Orange Book upon withdrawal of the patent information by the NDA holder could result in ANDA applicants withdrawing corresponding patent certifications prematurely and thus undermining a first applicant's exclusivity, FDA will leave information related to withdrawn patents in the Orange Book until it has determined that any related 180-day exclusivity has expired." FDA, Decision Letter, Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008), at 7 n.13.

[168] FDA, Request for Comments: Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (Sept. 26, 2007).

[169] In response to Cobalt's argument that the 30-month periods referenced in the failure to market and failure to obtain tentative approval forfeiture provisions do not begin to run until receipt of the first applicant's notice letter, FDA noted that while the start date for calculating the 30-month period under the tentative approval forfeiture provision is the date on which an ANDA application is "filed," the start date for calculating the 30-month period under the failure to market provision is the date of "submission" of the ANDA. The agency reasoned that because there is no evidence that Congress intended a difference between the two terms and because both terms are used in the context of "first applicant" status, it will interpret the terms "filed" and "submission" to refer to the date on which the agency determines an ANDA to be sufficiently complete to permit substantive review. FDA, Decision Letter, Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008), at 9 n.15. FDA further noted that when an ANDA is "determined, upon review, to have been substantially complete as of the day it was submitted to FDA, it will be deemed to have been received as of the date it was submitted (i.e., date-stamped by the appropriate FDA mail-room)." *Id.* at 6 n.10.

[170] Cobalt's ANDA was deemed substantially complete on March 22, 2005; 30 months from that date was September 22, 2007. Cobalt's ANDA was approved on May 7, 2008; the 75-day period would expire on July 21, 2008. Therefore, September 22, 2007, was the relevant date for the first prong of the failure to market analysis.

[171] Neither of the other possible triggering events (a final decision that the patent is invalid or not infringed, or a settlement order or consent decree entering final judgment that includes a finding that the patent was invalid or not infringed) had occurred.

[172] FDA noted that the D.C. Circuit stated in *Ranbaxy* that the "decisions rendered by FDA and the district court had been made pursuant to the Act 'as it stood before the MMA and, because the MMA was not made retroactive ... this decision is also geared to the Act pre-MMA).'" FDA, Decision Letter, Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008) (citing Ranbaxy Labs. Ltd. v. Leavitt, 469 F.3d 120, 122 (D.C. Cir. 2006)).

the agency concluded that between September 22, 2007, and June 30, 2007 (75 days after Bayer withdrew its patent on April 16, 2007), September 22, 2007, was also the "later of" date and thus was the controlling date. Because Cobalt failed to market its generic acarbose tablets by September 22, 2007, it forfeited its 180-day exclusivity. As a result, FDA also approved the ANDA submitted by a subsequent applicant, Roxane Laboratories.

FDA noted that it had "considered and rejected" comments by Cobalt that eligibility for 180-day exclusivity following the pioneer's voluntary withdrawal of its patent should be governed by *Ranbaxy*. In *Ranbaxy*, the D.C. Circuit held that "FDA may not condition the delisting of a patent on the existence of patent litigation, and thus deprive an ANDA applicant ...of a period of marketing exclusivity for which it would otherwise be eligible." According to FDA, the court in *Ranbaxy* "did not purport to render a decision on patent delisting and exclusivity under the MMA." And the new failure to market forfeiture provision specifically addresses the effect of patent delisting on eligibility for 180-day exclusivity for new ANDAs.[173]

ii. *Generic dorzolamide hydrochloride/timolol maleate.*

On October 11, 2005, Hi-Tech became the first applicant to submit a substantially complete ANDA for a generic version of Cosopt (dorzolamide hydrochloride/timolol maleate), an ophthalmic drug indicated for the treatment of ocular hypertension and open-angle glaucoma. Merck, the manufacturer of Cosopt, had listed three patents in the *Orange Book* for Cosopt. One of these patents was the '413 patent, which expired on April 28, 2008. Merck had obtained a period of pediatric exclusivity, which applied to the patent until October 28, 2008. The other two patents, the '735 patent and the '443 patent, expire on April 17, 2011. Hi-Tech submitted paragraph IV certifications for all three patents. Merck sued Hi-Tech only for infringement of the '413 patent. It also filed a statutory disclaimer of the '735 and '443 patents with the PTO, and it requested that FDA delist the patents from the *Orange Book*.

On the day before Merck made its delisting request, the district court entered final judgment on the pleadings in Merck's favor and ordered that the effective date of approval of Hi-Tech's ANDA could not occur prior to October 28, 2008, the expiration of the pediatric exclusivity period attached to the '413 patent.[174] The Federal Circuit affirmed.[175] Hi-Tech brought suit against FDA, seeking a declaratory judgment that its ANDA was entitled to 180-day exclusivity and seeking to enjoin FDA from granting final approval to any other ANDA for 180 days after Hi-Tech commenced marketing of its product, which it expected to do on October 28, 2008.[176]

According to Hi-Tech's brief, FDA had stated that it would not rule on Hi-Tech's exclusivity "until no earlier than October 28, 2008." Hi-Tech argued that because it was "simply not possible" for the company to wait until that date to file a lawsuit

[173] Cobalt brought suit against the agency but voluntarily dismissed its suit following denial of a TRO. Cobalt Labs. Inc. v. FDA, No. 08-cv-00798 (D.D.C. May 16, 2008) (notice of voluntary dismissal without prejudice).

[174] Merck & Co., Inc. v. Hi-Tech Pharmacal Co., Inc., Nos. 06-266 and 06-268, 2006 U.S. Dist. LEXIS 95820 (D.N.J. Apr. 25, 2006).

[175] Merck & Co., Inc. v. Hi-Tech Pharmacal Co., Inc., 482 F.3d 1317 (Fed. Cir. 2007).

[176] Hi-Tech Pharmacal Co., Inc. v. FDA, No. 08-cv-01495 (D.D.C. Aug. 28, 2008) (complaint). A motion to intervene as a defendant filed by Apotex, a subsequent ANDA filer, was granted by the district court on September 5, 2008.

and seek and obtain relief from the court if the agency "incorrectly decide[d]" that Hi-Tech was not entitled to 180-day exclusivity, it was entitled to relief "well before" October 28. Hi-Tech further argued that because there was no legal right to market prior to October 28 (the expiration of pediatric exclusivity relating to the '413 patent), there could be no finding of forfeiture based on failure to market. In addition, it asserted that the '735 and '443 patents had not and could not be withdrawn from the *Orange Book* in light of *Ranbaxy*. Therefore, according to Hi-Tech, the second prong of the failure to market provision could not have been satisfied. In response, FDA opened a docket and began collecting comment on the issue.[177]

Prior to the issuance of FDA's determination regarding forfeiture, the U.S. District Court for the District of Columbia denied Hi-Tech's request for a preliminary injunction because there had been no final agency action.[178] In an opinion filed October 10, 2008, the district court stated that "Hi-Tech is not entitled to judicial review of the interpretation and application of the exclusivity forfeiture provisions of the [MMA] until the FDA itself first interprets and applies those provisions with respect to Hi-Tech's ANDA." The court, however, requested that FDA "attempt to make a determination with respect to Hi-Tech's entitlement to exclusivity in advance of October 28, 2008."

On October 28, FDA announced that Hi-Tech had forfeited its eligibility for 180-day exclusivity on April 11, 2008.[179] As to each patent for which Hi-Tech submitted a paragraph IV certification initially qualifying it as a first applicant (the '413, '735, and '443 patents), the generic manufacturer either failed to lawfully maintain its paragraph IV certification or forfeited its exclusivity under the failure to market provision. First, FDA noted, Hi-Tech failed to lawfully maintain a paragraph IV certification with respect to the '413 patent because it lost its patent litigation as to that patent. Hi-Tech was required to change its paragraph IV certification to a paragraph III certification.[180] Second, Hi-Tech had forfeited its eligibility for exclusivity with respect to the '735 and '443 patents. For purposes of the first prong of the failure to market provision, April 11, 2008, was the "earlier of" date between the date that was 30 months from the date on which Hi-Tech submitted a substantially complete ANDA containing a paragraph IV certification to the patents and the date that was 75 days after FDA approved Hi-Tech's ANDA.[181] The triggering event under the second prong was Merck's request to delist the '735 and '443 patents on April 26, 2006. Based on this finding, FDA concluded that between April 11, 2008, and July 10, 2006 (75 days after Merck withdrew its patents), April 11, 2008, was the "later of" and thus the controlling date. Because Hi-Tech failed to market its generic version of Cosopt by April 11, 2008, it forfeited its eligibility for 180-day exclusivity.

FDA rejected Hi-Tech's argument that the agency "mishandled" Merck's request that the '735 and '443 patents be delisted. The agency explained that it has "imple-

[177] FDA, Request for Comments: Dorzolamide Hydrochloride/Timolol Maleate Tablets and 180-Day Exclusivity, Docket No. FDA-2008-N-0483 (Sept. 4, 2008).

[178] Hi-Tech Pharmacal Co., Inc. v. FDA, 587 F. Supp. 2d 1 (D.D.C. 2008).

[179] FDA, Decision Letter, Dorzolamide Hydrochloride/Timolol Maleate Tablets and 180-Day Exclusivity, Docket No. FDA-2008-N-0483 (Oct. 28, 2008).

[180] Although Hi-Tech did not submit its paragraph III certification to the '413 patent until April 10, 2008, as of June 11, 2007, when the Federal Circuit entered the mandate in the litigation involving the '413 patent, FDA stated that "Hi-Tech could no longer lawfully maintain its paragraph IV certification." *Id.* at 6.

[181] Hi-Tech's ANDA was deemed substantially complete on October 11, 2005; 30 months from that date was April 11, 2008. Hi-Tech's ANDA was approved on October 28, 2008; the 75-day period expired on January 11, 2009. Therefore April 11, 2008, was the relevant date for the first prong of the failure to market analysis.

mented the patent withdrawal provision [of the failure to market provision] so as to preserve 180-day exclusivity for first applicants by retaining that patent information in the *Orange Book* until the agency has determined that the first applicants with certifications to those patents have either used or forfeited the exclusivity period." According to the agency, if it were to immediately delist the patent upon a request by the NDA holder that the patent be withdrawn, this would result in an "immediate loss" of eligibility for 180-day exclusivity and would be "inconsistent" with the failure to market provision, which contemplates that, for at least 75 days after the patent is withdrawn, a first applicant will maintain its eligibility to begin its 180-day period of exclusivity. The agency again rejected the argument that eligibility for 180-day exclusivity following an NDA holder's voluntary withdrawal of its patent should be governed by "the rule established in *Ranbaxy*." According to FDA, the court in that case "did not purport to render a decision on patent delisting and exclusivity under the MMA." Although Hi-Tech brought suit, the court decided the case on the pediatric exclusivity issue, finding that the forfeiture clock had not been tolled during the pediatric exclusivity term as discussed above in section II. C. 3.,[182] and it never reached the delisting question.

4. *What is the effect of a first applicant's failure to market its generic product within 30 months of submitting its ANDA?*

With respect to old ANDAs, generally speaking there is no effect if the first applicant fails to market its generic product within 30 months of submitting its ANDA. This is one reason subsequent applicants have filed declaratory judgment actions, seeking to trigger the running of the 180 days.[183] For new ANDAs, however, the MMA contains a forfeiture provision based on an applicant's failure to market within 30 months of submitting its application.[184] FDA has interpreted this provision three times, confirming that two events must occur for forfeiture to happen: 1) 75 days must pass following an appellate court decision, settlement order, consent decree, or patent delisting, and 2) 30 months must pass following ANDA submission or 75 days must pass following effective ANDA approval.

In a matter involving generic granisetron hydrochloride, the agency declined to find forfeiture because—despite the applicant's failure to market within the statutory deadline—there had not yet been a court decision, court order or delisting. Teva was the first to file an ANDA seeking approval to market a generic version of 1 mg/mL single dose vials of Kytril (granisetron hydrochloride), an antinauseant and antiemetic drug. The ANDA, received for filing on June 1, 2004, contained a paragraph III certification for one patent that expired on December 29, 2007; a section viii statement as to a patent that expires on September 14, 2016; and the first paragraph IV certification for a patent that expires in 2019. Roche, the innovator, did not sue Teva for patent infringement, and FDA tentatively approved Teva's application on August 16, 2005. In a letter dated September 28, 2007, Teva requested that FDA confirm that it was entitled to 180-day exclusivity for its generic granisetron hydrochloride product.[185] It argued that even though more than 30 months had elapsed since it had submitted its ANDA, it had not forfeited its exclusivity because the possibility of a "later" forfeiture event under the failure to market provision—a court decision, court

[182] Hi-Tech Pharmacal Co., Inc. v. FDA, 587 F. Supp. 2d 13 (D.D.C. 2008).

[183] *See, e.g.*, Apotex Inc. v. Bristol-Myers Squibb Co., No. 04-cv-02922 (S.D.N.Y. Apr. 15, 2004) (complaint).

[184] 21 U.S.C. § 355(j)(5)(D)(i)(I).

[185] Letter from Marc A. Goshko, Executive Director, Teva North America, to Gary Buehler, Director, FDA Office of Generic Drugs, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Sept. 28, 2007).

order, or delisting—still remained. After opening a docket to solicit comments,[186] FDA agreed, approved the ANDA, and granted 180-day exclusivity.[187] No claim of infringement on the patent at issue had been brought against Teva or any subsequent applicant, nor had any ANDA applicant brought a declaratory judgment action regarding the patent. Consequently, no court had entered a final judgment of invalidity or non-infringement, and no court had signed a settlement order or consent decree entering final judgment of invalidity or non-infringement. In addition, Roche, the holder of the NDA for Kytril, had not requested that the patent be withdrawn from the *Orange Book*. None of these three possible events had occurred, the agency reasoned, so there was no forfeiture.

In a matter involving generic acarbose, the agency did find forfeiture for failure to market. As discussed above in section III. A. 3. b. i., Cobalt submitted an ANDA for a generic version of Precose (acarbose) tablets, along with a paragraph IV certification, on March 22, 2005. As the first filer, it was eligible for 180-day exclusivity. In a September 26, 2007 letter to applicants with pending ANDAs for generic acarbose tablets, FDA solicited comments regarding the applicability of the forfeiture provisions to Cobalt's eligibility for 180-day exclusivity. In May 2000, FDA approved Cobalt's ANDA but concluded that the manufacturer had forfeited its exclusivity on September 22, 2007, because the company did not begin to market its product by that date. The triggering event under the second prong of this forfeiture provision was Bayer's request to delist the Precose patent on April 16, 2007, and the matter is discussed in section III. A. 3. b. i. The agency similarly relied on delisting when it found forfeiture for failure to market in the generic dorzolamide hydrochloride/timolol maleate matter, discussed in section III. A. 3. b. ii. In this matter, FDA found that Hi-Tech forfeited exclusivity because more than 30 months had passed since the submission of its ANDA and because more than 75 days had passed since Merck requested the delisting of the relevant patents.

5. *What is the effect of failing to obtain tentative approval within 30 months after filing an ANDA?*

With respect to old ANDAs, generally speaking there is no effect if the first applicant fails to market its product within 30 months of submitting its ANDA. For new ANDAs, however, if an applicant fails to obtain tentative approval within 30 months after filing its ANDA (and the failure is not caused by a post-filing change in or a review of the ANDA approval requirements), the first applicant will forfeit exclusivity.[188] Even if a first applicant fails to obtain tentative approval within 30 months after filing its ANDA, however, FDA will not make a formal determination of forfeiture unless a subsequent applicant becomes eligible for approval within 180 days after the first applicant begins commercial marketing.[189]

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[186] FDA, Request for Comments: Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Oct. 11, 2007).

[187] FDA, Decision Letter, Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Jan. 17, 2008).

[188] 21 U.S.C. § 355(j)(5)(D)(i)(IV).

[189] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Sandoz Inc. 3 (July 31, 2006) (noting in approval letter for Sandoz's ANDA that the agency "is not making a formal determination at this time of Sandoz's eligibility for 180-day generic drug exclusivity" and "will do so only if another applicant becomes eligible for approval within 180 days after Sandoz begins commercial marketing of [its generic product]"); Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Perrigo R&D Co. 3 (Feb. 6, 2008) (noting in approval letter for Perrigo's ANDA that the agency "is not making a formal determination at this time of Perrigo's eligibility for 180-day generic drug exclusivity" and "will do so only if another applicant becomes eligible for approval within 180 days after Perrigo begins commercial marketing of [its generic product]").

As discussed above in sections III. A. 3. b. i., and III. A. 4., Cobalt forfeited its 180-day exclusivity for its generic acarbose tablets because 30 months had passed after the ANDA was deemed substantially complete and because 75 days had passed since Bayer delisted the patent. In the nonrulemaking docket that FDA opened for this matter, the agency also asked for comment on the effect of Cobalt's failure to obtain tentative approval within 30 months of filing its ANDA on its exclusivity. Ultimately, FDA determined that although Cobalt had forfeited its exclusivity under the failure to market provision, it had not forfeited its exclusivity because of its failure to obtain tentative approval within 30 months after filing its ANDA.[190] This forfeiture provision contains an exception if failure to obtain tentative approval is caused by a change in, or review of, the requirements for approval of the application imposed after the application was filed. Moreover, under amendments to the FDCA included in the Food and Drug Administration Amendments Act (FDAAA), Congress clarified that if approval of a first applicant's ANDA is delayed because of a petition, the 30-month period is extended by a period of time equal to the period beginning on the date on which the petition is received and ending on the date of final agency action on the petition.[191] Thus, the agency reasoned, because Cobalt had submitted petitions regarding the appropriate methodology for establishing bioequivalence for acarbose products[192] and because FDA changed its bioequivalence requirements with respect Cobalt's ANDA in August 2006,[193] Cobalt was subject to the exception. Therefore it did not forfeit exclusivity due to its failure to obtain tentative approval by September 22, 2007.

6. *What is the effect of a settlement agreement, terminating patent litigation, on the first applicant's eligibility for exclusivity?*

A settlement agreement terminating patent litigation has no effect on the ANDA applicant's 180-day exclusivity, unless a court signs a settlement order or consent decree finding a patent invalid or not infringed, or there is a final, unappealable order finding that the settlement agreement violates antitrust laws. Prior to the passage of the MMA in 2003, FDA concluded that a settlement agreement, which ended patent infringement litigation, effectively turned a paragraph IV certification into a paragraph III certification. A federal court in West Virginia held that

[190] As noted above, Cobalt's ANDA was sufficiently complete for review on March 22, 2005. The 30-month period for purposes of the failure to obtain tentative approval forfeiture provision therefore began on that date. It ended on September 22, 2007. Cobalt did not obtain tentative approval by that date.

[191] 21 U.S.C. § 355(q)(1)(G). According to FDA, the FDAAA makes clear that the failure to obtain tentative approval provision "gives a first applicant 30 months in which to obtain either tentative approval or approval." FDA, Decision Letter: Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008), at 10 n.17.

[192] Cobalt Laboratories Inc. and Cobalt Pharmaceuticals Inc., Citizen Petition and Emergency Petition for Stay of Action, Docket No. 2007P-0448 (FDA-2007-P-0418) (Nov. 9, 2007). In a separate response dated May 7, 2008, FDA denied Cobalt's request that all ANDA applicants conduct *in vivo* bioequivalence testing. It further denied Cobalt's request not to grant bioequivalence waivers to ANDA applicants. The agency, however, granted in part Cobalt's request that ANDA applicants conduct *in vivo* bioequivalence testing based on its determination that such testing is required if the test product is not qualitatively and quantitatively the same as the reference listed drug with respect to inactive ingredients. FDA, Response, Docket No. 2007P-0448 (FDA-2007-P-0418) (May 7, 2008), at 10-11.

[193] Cobalt originally conducted its bioequivalence study using the 100 mg strength tablets. It was advised by the agency on August 8, 2006, that its *in vivo* bioequivalence study using that strength was not acceptable. As a result, Cobalt relied on a different strength of acarbose tablets for its *in vivo* bioequivalence study. FDA, Decision Letter: Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008), at 11.

the agency's decision on this issue was unreasonable. Congress addressed this issue in the 2003 legislation by adding two forfeiture provisions related to settlements. Under the failure to market provision, if 75 days have passed since approval of the first applicant's ANDA was made effective (or 30 months have elapsed since the first applicant's ANDA was submitted), then if a court signs a settlement order or consent decree that enters a final judgment finding the last of the patents qualifying it for exclusivity invalid or not infringed, the first applicant will forfeit exclusivity if it fails to market within 75 days.[194] Under a separate forfeiture provision, a first applicant will also lose its exclusivity if there is an unappealable order finding that a settlement agreement violates antitrust laws.[195] This second provision was retroactive, applying to first ANDAs filed before passage of the MMA and pending at the agency at the time of enactment.[196]

Since the authors' last article, FDA declined to find forfeiture in a case involving an old ANDA where there had not been a final, unappealable order that the agreement violated antitrust law. In two matters pending at the time this article was written, the FTC alleges that various settlement agreements violate the antitrust laws. If these are confirmed by the court, they could result in the first forfeitures under the forfeiture provision for settlement agreements determined to violate the antitrust laws. There have been no petitions, or, to the authors' knowledge, court cases involving interpretation of the failure to market forfeiture provision with respect to settlements.

a. *Pre-MMA.*

The authors discussed the first settlement case in their prior article (and above in section II. C. 1.) Mylan was the first ANDA applicant to submit a paragraph IV certification to the 30 mg dosage of Procardia XL (nifedipine extended release). Pfizer, the manufacturer of Procardia, sued Mylan for infringement, and the parties settled in February 2000. Although the settlement terms were not disclosed, Pfizer licensed Mylan to sell a private label version of its own 30 mg, 60 mg, and 90 mg nifedipine extended release products. Pfizer may also have permitted Mylan to market its own 30 mg product under its own ANDA, but Mylan never did so. In response to a petition submitted by Teva, a generic manufacturer, asking FDA to determine if Mylan's ANDA was eligible for exclusivity,[197] FDA concluded that Mylan was not eligible for exclusivity.[198] It reasoned, in part, that the settlement effectively turned Mylan's paragraph IV certification into a paragraph III certification. Mylan brought suit. In the decision that resulted, the district court in West Virginia, while upholding the case on other grounds discussed above in section II. C. 1., found this unreasonable.[199] The court was not prepared to allow FDA unilaterally to deem the paragraph IV certification to be a paragraph III certification, simply on account of the settlement.

b. *Post-MMA.*

In a case involving a settlement agreement relating to generic ramipril, after opening a docket to consider the forfeiture question, FDA concluded it had no

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[194] 21 U.S.C. § 355(j)(D)(i)(I).

[195] 21 U.S.C. § 355(j)(D)(i)(V).

[196] *See* Pub. L. No. 108-173 § 1102(b)(2), 117 Stat. 2066, 2460 (2003) ("(2) COLLUSIVE AGREEMENTS.—If a forfeiture event described in section 505(j)(5)(D)(i)(V) of that Act occurs in the case of an applicant, the applicant shall forfeit the 180-day period under section 505(j)(5)(B)(iv) of that Act without regard to when the first certification under section 505(j)(2)(A)(vii)(IV) of that Act for the listed drug was made.")

[197] Teva Pharmaceuticals USA, Inc., Citizen Petition, Docket No. 2000P-1446 (Aug. 9, 2000).

[198] FDA, Response, Docket No. 2004P-1446 (Feb. 6, 2001), at 1.

[199] Mylan Pharms., Inc. v. Thompson, 207 F. Supp. 2d 476, 487 (N.D. W.Va. 2001).

discretion to find forfeiture absent a final order on the antitrust question. Cobalt submitted the first ANDA with a paragraph IV certification for generic versions of 1.25 mg, 2.5 mg, 5 mg, and 10 mg Altace (ramipril) capsules on November 26, 2002. It was, therefore, a first applicant subject to the old ANDA provisions, but—as noted—the settlement agreement forfeiture provision was retroactive. Aventis and King Pharmaceuticals, owner of the composition of matter patent and holder of the NDA for Altace (respectively), sued Cobalt for patent infringement. In March 2004, the three parties signed a stipulation in which Cobalt admitted to infringement of the patent at issue.[200] Cobalt reserved its invalidity and unenforceability defenses. In April 2006, a district court in Massachusetts granted a stipulation of dismissal submitted by Aventis, King Pharmaceuticals, and Cobalt, voluntarily dismissing the patent litigation without prejudice.[201] Prior to settlement, the 30-month stay had expired, and FDA had granted final approval to Cobalt's ANDA, although Cobalt had not yet begun to market its product. The settlement agreement was submitted to the FTC.

On March 18, 2005, Lupin Pharmaceuticals submitted a subsequent ANDA with a paragraph IV certification to the same patent. Aventis and King Pharmaceuticals sued Lupin for patent infringement, and on September 11, 2007, the Federal Circuit invalidated the patent claims at issue.[202] Before the court issued its mandate, FDA received a letter from Lupin and a letter from Hyman, Phelps & McNamara on behalf of an unidentified generic manufacturer challenging Cobalt's eligibility for 180-day exclusivity. Lupin claimed that because of the settlement agreement between Cobalt, King, and Aventis, Cobalt was no longer entitled to 180-day exclusivity. According to Lupin, the settlement rendered Cobalt's paragraph IV certification inaccurate because Cobalt had ceased asserting that the patent in question was invalid. Lupin further argued that Cobalt was "unwilling to stand behind its initial opinion" that the patent at issue was invalid and unenforceable, because Cobalt had not yet marketed its approved generic ramipril product. Lupin cited the nifedipine matter discussed above, where FDA had found that Mylan had effectively converted its paragraph IV certification to a paragraph III because Mylan had settled the suit and failed to market nifedipine.[203] Hyman Phelps made similar arguments.

After FDA established a docket for comments,[204] the Federal Circuit's mandate issued, and Cobalt began commercial marketing of its ramipril capsules. Shortly thereafter, FDA informed Lupin that Cobalt was entitled to 180-day exclusivity, which was triggered with the issuance of the Federal Circuit's mandate.[205] The agency pointed out that the settlement agreement forfeiture provision was retroactive and therefore applies to old ANDAs, such as Cobalt's ANDA. FDA also noted that "Congress did not provide for such a forfeiture as the result of any other type of settlement for ANDAs otherwise governed by" the old provisions. The agency

[200] Aventis Pharma Deutschland GMBH v. Cobalt Pharms., Inc., No. 03-10492 (D. Mass. Mar. 24, 2004) (stipulation).

[201] Aventis Pharma Deutschland GMBH v. Cobalt Pharms., Inc., No. 03-10492 (D. Mass. Apr. 4, 2006) (stipulation of dismissal).

[202] Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293 (Fed. Cir. 2007).

[203] Lupin stated that FDA did not have the opportunity to appeal the West Virginia district court's conclusion that the agency's determination in the nifedipine case was unreasonable because the agency prevailed on other grounds.

[204] FDA, Request for Comments: Ramipril Capsules and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0382 (Docket No. FDA-2007-N-0035) (Oct. 3, 2007).

[205] FDA, Decision Letter, Ramipril Capsules and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0382 (Docket No. FDA-2007-N-0035) (Jan. 29, 2008).

concluded that because there was no final, unappealable order finding that the settlement agreement violates antitrust laws, Cobalt did not forfeit its exclusivity as a result of the settlement agreement.[206]

In two cases pending at the time this article was written, the FTC was asserting that settlement agreements involving generic modafinil and generic testosterone gel violate the antitrust laws.

On December 24, 2002, Teva, Ranbaxy, Mylan and Barr each filed an ANDA containing a paragraph IV certification with respect to one of two listed patents for Provigil (modafinil).[207] This made the four manufacturers eligible for shared 180-day exclusivity, and their ANDAs were governed by the old provisions. The patent in question expires in October 2014.[208] The NDA holder, Cephalon, sued all four generic manufacturers for patent infringement, and the stay triggered by the lawsuit expired in June 2006. FDA tentatively approved Barr's ANDA on January 7, 2004, Ranbaxy's ANDA on February 18, 2004, Mylan's ANDA on February 9, 2005, and Teva's ANDA on December 16, 2005. Between December 2005 and February 2006, Cephalon entered into settlement agreements and signed joint stipulations dismissing the infringement lawsuit with all four generic manufacturers.[209] According to the FTC, as part of the settlement agreements, Cephalon "compensated each generic company ... to abandon its patent challenge and agree to forgo entry until April 2012."[210]

On February 13, 2008, the FTC filed a complaint in the U.S. District Court for the District of Columbia seeking a permanent injunction against Cephalon for "unfair methods of competition" in violation of section 5(a) the Federal Trade Commission Act (FTCA).[211] The FTC alleges that Cephalon engaged in anticompetitive conduct by inducing the four generic companies to end their patent challenges and refrain from selling a generic version of Provigil until 2012 in exchange for payments totaling more than $200 million.[212] Because Teva, Ranbaxy, Mylan and Barr share 180-day exclusivity, the FTC further contends that Cephalon, in making these agreements, has blocked competition by any other generic entrant as well. Although the FTC did not sue Teva, Ranbaxy, Mylan and Barr, these generic manufacturers apparently will forfeit 180-day exclusivity if there is a final, unappealable decision of the court that the settlements at issue are unfair methods of competition and thus violate section 5 of the FTCA.[213]

The second action brought by the FTC concerns a settlement agreement involving AndroGel (testosterone gel). On May 13, 2003, Watson became the first applicant to file an ANDA containing a paragraph IV certification to market a generic version of Solvay's AndroGel (testosterone gel).[214] Paddock filed a separate ANDA

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[206] FDA also concluded that Cobalt's paragraph IV certification remained appropriate, because Cobalt sought and obtained approval to market its ramipril capsule products prior to patent expiry.

[207] FTC v. Cephalon, Inc., No. 08-cv-00244, at 9 (D.D.C. Feb. 13, 2008) (complaint).

[208] Cephalon, the NDA holder, has also received pediatric exclusivity.

[209] Cephalon, Inc. v. Mylan Pharm., Inc., No. 03-cv-1394 (D. N.J. Dec. 9, 2005) (joint stipulation for dismissal with prejudice signed by Cephalon and Teva); Cephalon, Inc. v. Mylan Pharm., Inc., No. 03-cv-1394 (D. N.J. Dec. 22, 2005) (joint stipulation for dismissal with prejudice signed by Cephalon and Ranbaxy); Cephalon, Inc. v. Mylan Pharm., Inc., No. 03-cv-1394 (D. N.J. Jan. 12, 2006) (joint stipulation for dismissal with prejudice signed by Cephalon and Mylan); Cephalon, Inc. v. Mylan Pharm., Inc., No. 03-cv-1394 (D. N.J. Feb. 2, 2006) (joint stipulation for dismissal with prejudice signed by Cephalon and Barr).

[210] FTC v. Cephalon, Inc., No. 08-cv-00244, at 2 (D.D.C. Feb. 13, 2008) (complaint).

[211] FTC v. Cephalon, Inc., No. 08-cv-00244 (D.D.C. Feb. 13, 2008) (complaint).

[212] *Id.* at 1-2, 14.

[213] *See* 21 U.S.C. § 355(j)(5)(D)(i)(V).

[214] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Watson Laboratories, Inc. 1 (Jan. 27, 2006).

later that same month.[215] Paddock subsequently entered into an agreement with Par, which provided that Par would share litigation costs with Paddock, market Paddock's generic testosterone gel, and share in any resulting profits.[216] Solvay sued Watson and Paddock for patent infringement in August 2003, triggering 30-month stays of approval with respect to both ANDAs.[217] The stays expired in January 2006.[218] Shortly thereafter, on January 27, 2006, FDA granted final approval to Watson's ANDA.[219] On September 13, 2006, Solvay, Watson and Paddock (along with Par) entered into separate settlements agreements.[220] Under these agreements, Watson, Paddock and Par agreed to refrain from marketing their generic products until August 31, 2015, or earlier if another generic company launched a generic product prior to that date.[221] The agreements also included co-promotion deals and profit sharing. In addition, Solvay and Par agreed to a back-up manufacturing arrangement.[222]

On January 27, 2009, the FTC filed a complaint in the U.S. District Court for the Central District of California alleging, in part, that the agreements constitute "unfair method[s] of competition" in violation of section 5(a) of the FTCA.[223] The FTC contends that Solvay, Watson, Paddock and Par acted unlawfully when "Solvay paid Watson and Par a share of its AndroGel profits to abandon their patent challenges and agree to delay generic entry until 2015."[224] If there is a final, unappealable decision of the court that the settlement between Solvay and Watson constitutes an unfair method of competition and thus violates section 5 of the FTCA, Watson could forfeit its exclusivity if it has not already launched its generic product.[225]

B. *Observations on Forfeiture*

1. *Impact of the 30-Month Stay on the Failure to Market Provision*

One observer has suggested that first applicants subject to the statutorily mandated 30-month stay[226] will likely be unable to obtain final approval within 30 months of ANDA submission.[227] Because the first prong of the failure to market

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[215] FTC v. Watson Pharms., Inc., No. 09-cv-00598, at 11 (C.D. Cal. Jan. 27, 2009) (complaint).

[216] *Id.*

[217] *Id.* at 11-12.

[218] *Id.* at 12.

[219] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Watson Laboratories, Inc. 1 (Jan. 27, 2006).

[220] FTC v. Watson Pharms., Inc., No. 09-cv-00598, at 16, 18 (C. D.Cal. Jan. 27, 2009) (complaint).

[221] *Id.*

[222] Par also "agreed to transfer $6 million up front to Paddock through a transfer of title of Paddock's ANDA to Par." *Id.* at 19.

[223] *Id.* at 27.

[224] Press Release, FTC, FTC Sues Drug Companies for Unlawfully Conspiring to Delay the Sale of Generic AndroGel Until 2015 (Feb. 2, 2009), *available at* http://www.ftc.gov/opa/2009/02/androgel.shtm.

[225] *See* 21 U.S.C. § 355(j)(5)(D)(i)(V).

[226] If the NDA holder or patent owner brings an infringement action within 45 days of receiving notice of the paragraph IV certification, there will be a 30-month stay of final approval of the application "beginning on the date of the receipt of the notice," unless a final decision is reached earlier in the patent case or the court hearing the case orders a longer or shorter period. 21 U.S.C. § 355(j)(5)(B)(iii).

[227] This observation was made by Robert A. Dormer at a FDLI conference on the Hatch-Waxman amendments on February 5, 2009. *See* Robert A. Dormer, 180-Day Exclusivity Forfeiture Mechanics, FDA Decisions, and Recent Court Decisions, Presentation at FDLI's Waxman-Hatch: Back to the Future (Feb. 5, 2009) (stating that "30-month stay of approval under section 505(j)(5)(A)(iii) for paragraph IV litigation does not begin until approximately 80 days after submission of ANDA, making it unlikely that an applicant will get approval within 30 months of submission").

provision is triggered by the earlier of 75 days after the date on which approval of its application is effective, or 30 months after "the date of submission" of its application,[228] any delay in approval of an ANDA application beyond 30 months after submission could result in a forfeiture event.

As this observer explained, it is possible that the 30-month stay will not begin until 80 days after submission of an ANDA. For purposes of interpreting this provision, FDA considers the date an ANDA containing a paragraph IV certification is submitted to be the date the agency "received" the ANDA.[229] Under FDA's regulations, the agency has up to 60 days to determine if it will file, or in other words accept, an ANDA.[230] Once it makes this determination, the applicant has 20 days after the date of the postmark on the notice from FDA informing it that the ANDA has been filed to provide notice of its paragraph IV certification to the patent owner or NDA holder.[231] The 30-month stay is counted from the date of receipt of the notice of the paragraph IV certification.[232] As a result, it is conceivable that the 30-month stay will not begin until 80 days or even slightly longer after the application has been submitted.

Because FDA may not grant final approval to an ANDA during the 30-month stay if the patent infringement litigation is ongoing, it is possible that an ANDA applicant will not obtain final approval until more than 30 months after submission of its ANDA. If, in the meantime, the second prong of the failure to market provision has been triggered (for example, if a court in a separate infringement action involving a subsequent applicant finds the patent at issue invalid or not infringed), the 30-month lapse since submission will satisfy the first prong—triggering forfeiture before the ANDA could be approved and the product could ever be marketed.

2. *Possibility of "Parking"*

When Congress amended the FDCA in 2003 to add provisions for forfeiture of 180-day exclusivity, one Senator stated that it did so to "ensure that the 180-day exclusivity period enjoyed by the first generic to challenge a patent cannot be used as a bottleneck to prevent additional generic competition."[233] As some have noted, FDA's decisions in the granisetron and ramipril matters discussed above in sections III. A. 4. and III. A. 6. b., respectively, indicate that bottlenecks caused by a delay in marketing by the first applicant, often referred to as "parking," can theoretically occur under the new provisions despite the addition of the forfeiture provisions.[234]

The agency acknowledged the possibility of parking in its granisetron decision, discussed above in section III. A. 4. In that matter, FDA concluded that Teva did not forfeit its exclusivity because, even though an event under the first prong of the failure to market provision had occurred, none of the events under the second

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[228] 21 U.S.C. § 355(j)(5)(D)(i)(I)(aa).

[229] FDA, Decision Letter, Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Jan. 17, 2008), at 4 n.4; FDA, Decision Letter: Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 7, 2008), at 6 n.10.

[230] 21 C.F.R. § 314.101(a).

[231] 21 U.S.C. § 355(j)(2)(B)(ii)(I).

[232] 21 U.S.C. § 355(j)(5)(B)(iii).

[233] 149 Cong. Rec. 31,200 (2003) (statement of Sen. Schumer).

[234] *See, e.g., Recent Exclusivity Rulings Favor Generic Filers*, GENERIC LINE, Apr. 2, 2008.

prong had occurred.[235] Although FDA indicated that Teva, the first filer, had not parked its exclusivity, it stated in a footnote that:

> [i]nherent in the structure of the "failure to market" forfeiture provisions is the possibility that a first applicant would be able to enter into a settlement agreement with the NDA holder or patent owner in which a court does not enter a final judgment of invalidity or non-infringement (i.e. without a forfeiture event under subpart (bb) occurring), and that subsequent applicants would be unable to initiate a forfeiture with a declaratory judgment action.[236]

The agency further explained that, under these circumstances, the approval of an otherwise approvable ANDA, submitted by a subsequent applicant who would market its generic product if it could obtain approval, could be delayed.[237] As FDA noted, however, "[t]his potential scenario is not one for which the statute currently provides a remedy."[238]

One of the situations FDA foreshadowed in its granisetron decision as a potential barrier to triggering forfeiture occurred in the ramipril case. In this matter, as described above in section III. A. 6. b., Cobalt submitted the first ANDA with a paragraph IV certification for different strengths of generic Altace (ramipril) capsules. Aventis and King Pharmaceuticals sued Cobalt for patent infringement, and the parties signed a stipulation agreement in which Cobalt admitted its generic ramipril products would infringe the patent at issue. Cobalt, however, reserved its invalidity and unenforceability defenses. Lupin, a subsequent ANDA applicant, argued that the "settlement rendered [Cobalt's] paragraph IV certification inaccurate."[239] FDA rejected this argument.[240] As noted, because there was no final, unappealable order finding that the settlement agreement violates antitrust laws, Cobalt did not forfeit its exclusivity as a result of the settlement agreement. FDA therefore denied a request by Lupin, a subsequent applicant, to immediately approve its ANDA. Thus Cobalt holds the exclusivity, which will not be triggered until commercial marketing or a final, unappealable court decision holding the patent invalid or not infringed, and Lupin cannot avail itself of the settlement agreement forfeiture provision in light of FDA's decision or the failure to market forfeiture provision (because this provision does not apply to old ANDAs such as Cobalt's).

It is unclear how common the parking scenario will be in the future, however, in light of other developments in the law, including potentially greater availability of declaratory judgments in the wake of *MedImmune*.

3. *Timing of Forfeiture Decisions*

In two matters, in 2006 and 2008, respectively, it became apparent that FDA will not make a formal determination of forfeiture unless a subsequent applicant becomes eligible for approval within 180 days after the first applicant begins com-

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[235] FDA Decision Letter: Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Jan. 17, 2008), at 5.

[236] *Id.* at 5 n.6.

[237] *Id.*

[238] *Id.*

[239] FDA, Decision Letter: Ramipril Capsules and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0382 (FDA-2007-N-0035) (Jan. 29, 2008), at 5.

[240] *Id.*

mercial marketing. The first involved generic extended release metoprolol succinate, and the second involved generic famotidine.

Sandoz was the first applicant to submit an ANDA with a paragraph IV certification to market a generic version of 25 mg Toprol-XL (metoprolol succinate) Extended Release Tablets. Although FDA stated in its July 2006 approval letter that Sandoz failed to obtain tentative approval of its ANDA within 30 months after the date on which the ANDA was filed, the agency noted that it would not make a formal determination of eligibility for 180-day exclusivity at that time and would do so only if another ANDA applicant became eligible for approval within 180 days after Sandoz began marketing its product.[241] In a February 2008 letter approving Perrigo's ANDA to market a generic version of Merck's Pepcid Complete (famotidine 10 mg, calcium carbonate 800 mg, and magnesium hydroxide 165 mg) chewable tablets, the agency made the same comment.[242] Although Perrigo had failed to obtain tentative approval of its ANDA within 30 months of filing, the agency stated it would not make a formal determination as to whether Perrigo was eligible for 180-day exclusivity unless another applicant became eligible for approval within 180 days after Perrigo began commercial marketing of generic Pepcid Complete.

By way of contrast, on February 20, 2008, the agency approved an ANDA submitted by Watson to market a generic version of Camptosar (irinotecan hydrochloride) Injection , 20 mg/mL, and made a determination of forfeiture because there were other ANDAs pending. Although FDA determined that Watson was the first applicant to submit an ANDA with a paragraph IV certification for Camptosar Injection, it noted that Watson did not obtain tentative approval of its ANDA within 30 months after submission and thus forfeited the 180-day period of exclusivity.[243] Other ANDAs were ready for approval, and on February 27, the agency approved seven other applications for generic irinotecan hydrochloride injections.

4. *Prospect of Litigation*

A review of FDA's judicial record since it began facing challenges to its decisions relating to 180-day exclusivity indicates that federal courts have played an active role in shaping the interpretation of the provisions, particularly the old provisions. Based on our review of published and unpublished court cases, FDA's interpretation of the 180-day exclusivity provision in matters involving the old provisions has been litigated on 24 occasions.[244] The agency's decisions have been successfully challenged slightly over one third of the time. Given FDA's failure to conduct rulemaking and its practice of addressing interpretative issues with respect to the new provisions on a case-by-case basis, some have suggested that the courts will have an even greater role in shaping the application of the 180-day exclusivity provision with respect to

[241] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Sandoz Inc. 2 (July 31, 2006).

[242] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Perrigo R&D Co. 2-3 (Feb. 6, 2008).

[243] Letter from Gary Buehler, Director, FDA Office of Generic Drugs, to Watson Laboratories, Inc. 2 (Feb. 20, 2008).

[244] The authors excluded all decisions in which no ruling on the merits appears, including dismissals on procedural grounds and on jurisdictional grounds, as well as voluntary dismissals. The authors also excluded cases brought against FDA *pro se* and employment discrimination lawsuits. In addition, the authors excluded enforcement cases brought by the agency.

the new provisions, and in particular, the forfeiture provisions.[245] As of the end of February 2009, FDA had made forfeiture determinations on five occasions.[246] Before making its decision on four of these five occasions, FDA opened a nonrulemaking docket and sought comments from interested parties. The agency concluded that the first applicant had forfeited its exclusivity in three instances. Two of these rulings, the acarbose and dorzolamide hydrochloride/timolol maleate decisions, were challenged in court by the first applicant. The first applicant in the acarbose matter voluntarily dismissed its lawsuit after the court denied its motion for a TRO to prevent the approval of other ANDAs. The first applicant in the dorzolamide hydrochloride/timolol maleate decision carried its lawsuit further, seeking a decision on the merits. The district court deciding that case concluded that FDA's decision was reasonable based on the agency's interpretation of the pediatric exclusivity provisions. As a result, no court has yet interpreted the forfeiture provisions.

The fact that two of FDA's three decisions finding forfeiture have faced court challenges suggests that the agency's practice of deciding these issues on a case-by-case basis will likely lead to litigation. Some observers, however, have indicated that FDA's policy of waiting until an ANDA is ready for final approval to make a determination of eligibility for exclusivity could, in fact, deny the first filer any opportunity for meaningful judicial review.[247] The agency, by not informing a first applicant of its decision that the first applicant has forfeited its eligibility for 180-day exclusivity until it is ready to approve a subsequent ANDA, may deny that applicant a meaningful opportunity to challenge the determination of forfeiture. Once a subsequent ANDA applicant launches its product, the value of 180-day exclusivity is diminished.

Only one first applicant of a new ANDA thus far has brought a lawsuit seeking to force FDA to make an advance exclusivity determination, and it did so without success. As discussed above in section III. A. 3. b. ii., Hi-Tech argued that it was "simply not possible" for the company to wait until the date on which the period of pediatric exclusivity blocking ANDA approval ended to file a lawsuit and seek and obtain relief from the court if FDA "incorrectly decide[d]" that Hi-Tech was not entitled to 180-day exclusivity and a subsequent applicant entered the market. FDA defended its practice by asserting, as it has in its decision letters, that the approach it has adopted "is necessary because of the many factors that may influence eligibility for exclusivity up to the time an application is ready for approval (e.g. patent expiration, patent delisting, failure to obtain a tentative approval within 30 months, withdrawal of ANDA) and could thus render a premature eligibility de-

[245] For example, this observation was made by Robert A. Dormer at a FDLI conference on the Hatch-Waxman amendments on February 5, 2009. *See* Robert A. Dormer, 180-Day Exclusivity Forfeiture Mechanics, FDA Decisions, and Recent Court Decisions, Presentation at FDLI's Waxman-Hatch: Back to the Future (Feb. 5, 2009) (stating in this slide presentation that the "[t]rend of deciding on case-by-case basis often leaves it to the court to decide").

[246] As discussed above in section III. B. 3., on two other occasions FDA noted that although the first filers had failed to obtain tentative approval of their respective ANDAs within 30 months after the date on which the applications were filed, the agency would not make a formal determination as to whether the companies were eligible for 180-day exclusivity unless another applicant became eligible for approval within 180 days after they began to market their products.

[247] For example, this observation was made by Robert A. Dormer at a FDLI conference on the Hatch-Waxman amendments on February 5, 2009. *See* Robert A. Dormer, 180-Day Exclusivity Forfeiture Mechanics, FDA Decisions, and Recent Court Decisions, Presentation at FDLI's Waxman-Hatch: Back to the Future (Feb. 5, 2009) (noting in this slide presentation that FDA's policy regarding advance exclusivity determinations "can preclude meaningful judicial review of FDA decisions").

termination incorrect."[248] FDA also argued that its policy of not making forfeiture decisions prior to the approval of an ANDA is "consistent with Congress's choice to vest FDA with the authority to take and give effect to its actions, such as approving drugs, subject to subsequent challenge under the Administrative Procedure Act."[249] The district court denied Hi-Tech's request because there had been no final agency action. The court, however, required FDA to notify it and Hi-Tech at least 12 hours prior to release of the agency decision.

In light of this outcome, it is uncertain whether future first applicants will be able to force FDA to make exclusivity determinations prior to ANDA approval. It is possible that other courts could arrive at a different conclusion than the *Hi-Tech* court and expect FDA to make an earlier determination of potential eligibility. For instance, a court could require the agency to, at a minimum, make a determination that a forfeiture event has not yet occurred.

Given the lack of judicial precedent with respect to the forfeiture provisions, it is difficult to predict whether any future first applicants will challenge in court FDA determinations of forfeiture, particularly if the agency contemporaneously approves the ANDA of a subsequent filer. If, however, other first applicants continue to seek judicial relief from a determination of forfeiture and courts reach the merits of these cases, it is uncertain whether the highly deferential standard of review accorded under *Chevron USA, Inc. v. Natural Resources Defense Council, Inc.*,[250] will be granted to FDA's decisions given the absence of rulemaking with respect to the forfeiture provisions.[251]

IV. CONCLUSION

A. *The Impact of 180-Day Exclusivity*

While a fairly significant body of research exists examining the impact of generic drugs on drug prices and market shares, surprisingly there appears to be limited research regarding the economic effects of paragraph IV certifications and 180-day exclusivity on generic competition outside the context of authorized generics and patent settlement payments.

The Hatch-Waxman amendments, by reducing the costs of developing generic drugs through the creation of an abbreviated approval process and by offering incentives to generic manufacturers, are viewed as partly responsible for the increasing number of generic drugs in the marketplace.[252] The increase in generic

[248] Consolidated Memorandum in Support of Defendant's Motion to Dismiss and in Opposition to Plaintiff's Motion for Preliminary Injunction, Hi-Tech Pharmacal Co., Inc. v. FDA, No. 08-1495 (JDB), at 6 (D.D.C. Sept. 18, 2008).

[249] FDA's Status Report, Hi-Tech Pharmacal Co. Inc. v. FDA, No. 08-1495, at 2 (D.D.C. Oct. 24, 2008) (citation omitted).

[250] 467 U.S. 837 (1984).

[251] *Cf.* United States v. Mead Corp., 533 U.S. 218, 226-27 (2001) ("We hold that administrative implementation of a particular statutory provision qualifies for *Chevron* deference when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law, and that the agency interpretation claiming deference was promulgated in the exercise of that authority."); Christensen v. Harris County, 529 U.S. 576, 587 (2000) ("Interpretations such as those in opinion letters—like interpretations contained in policy statements, agency manuals, and enforcement guidelines, all of which lack the force of law—do not warrant *Chevron*-style deference.")

[252] *See, e.g.*, Anish Vaishnav, *The Impact of "Authorized Generics" on Independent Generic Entry: A Propensity Score Approach* 4 (Dec. 2007) *available at* http://emlab.berkeley.edu/econ/ugrad/theses/anish_vaishnav.pdf; *see also* FTC, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* i (July 2002) ("Beyond any doubt, Hatch-Waxman has increased generic drug entry."), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf.

drug availability and use has been paralleled by a rise in the number of ANDAs containing paragraph IV certifications. According to the FTC, from 1984 to 1989, only two percent of ANDAs contained paragraph IV certifications.[253] That figure, however, grew to approximately 12 percent for the 1990s, and it increased to 20 percent from 1998 to 2000.[254] In addition, the FTC has found, perhaps not surprisingly, that paragraph IV certifications often target brand name products with large markets.[255]

Some believe the increase in paragraph IV challenges may be linked in part to evolution of the rules governing 180-day exclusivity.[256] Prior to 1998, FDA granted 180-day exclusivity to only three ANDA applicants.[257] As discussed above in section II.B.1., in response to a court decision in 1998, *Mova Pharmaceutical Corp. v. Shalala*,[258] the agency abandoned its position requiring the first generic filer to successfully defend its paragraph IV challenge before earning 180-day exclusivity. In 2000, in the wake of another court decision, *Mylan Pharmaceuticals, Inc. v. Shalala*,[259] described above in section II. B. 3. a., FDA once again modified its interpretation of the statute and began reading the court decision trigger to allow the first filer to enter the market after a favorable district court decision instead of waiting for an appellate court decision.[260] Between 1998 to 2002, FDA awarded 180-day exclusivity to ANDA applicants for 31 drug products.[261] By July 2003, more than 60 ANDAs had received an award of 180-day exclusivity.[262] In 2003, FDA began allowing multiple applicants to share exclusivity for the same product if they delivered their ANDAs on the same day to agency.[263]

This rise in paragraph IV certifications and awards of 180-day exclusivity appears to reflect the belief by at least some generic manufacturers that first filers have advantages over subsequent filers.[264] For example, commentators have noted that the first ANDA applicant may charge higher prices during the period of exclusivity because of the lack of generic competition.[265] An analysis of single ingredient brand name and generic drugs sold in the United States from 1999 through 2004 conducted for FDA provides support for this observation. This analysis found that the first generic manufacturer in the market, on average, sold its product at a

[253] FTC, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* 10 (July 2002), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf.

[254] *Id.*

[255] *Id.* at ii (noting that "[t]he brand-name products included in the study represent[ed] some of the largest drug products as measured by annual sales").

[256] *See* Ernst R. Berndt, et al., *Do Authorized Generic Drugs Deter Paragraph IV Certifications? Recent Evidence* 5 (Apr. 2007) (working paper).

[257] FTC, *Generic Data Entry Prior to Patent Expiration: An FTC Study* vi (July 2002), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf. Between 1992 and 1998, FDA did not award exclusivity to any first filers. *Id.*

[258] 140 F. 3d 1060 (D.C. Cir. 1998).

[259] 81 F.Supp.2d 30 (D.D.C. 2000).

[260] For old ANDAs, the MMA codified FDA's previous reading of the court decision trigger as beginning when a decision is rendered by "a court from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken." As noted above, in section II. B. 3. b., there is no court decision trigger for exclusivity for new ANDAs, but a similar rule applies to a forfeiture event.

[261] Ernst R. Berndt, et al., *Do Authorized Generic Drugs Deter Paragraph IV Certifications? Recent Evidence* 5 (Apr. 2007) (working paper) (citation omitted).

[262] FDA, Guidance for Industry, 180-Day Exclusivity when Multiple ANDAs Are Submitted on the Same Day 3 n.4 (July 2003), *available at* http://www.fda.gov/CDER/guidance/5710fnl.pdf.

[263] As noted above, in section II. A. 2. b., the MMA codified the agency's decision.

[264] *See, e.g.*, Kevin A. Hassett, & Robert J. Shapiro, *The Impact of Authorized Generic Pharmaceuticals on the Introduction of Other Generic Pharmaceuticals* 6 (Apr. 2007), *available at* http://www.authorizedgenerics.com/downloads/ImpactofAuthorizedGenericPharmaceuticals.pdf.

[265] *Id.*

price that was only six-percent lower than the brand-name price.[266] Once a second generic competitor entered the market, the average generic price fell precipitously to almost half of the brand name price.[267] The average generic price continued to decline, but at a slower rate, as other generic products entered the market.[268] For products with 12 generic competitors, the average generic price was only 20 percent of the branded price.[269] In light of the average selling price of the first generic drug in the market, some have estimated that a first filer awarded 180-day exclusivity could, in fact, "expect a 1,000 percent return on investment."[270] In addition, first filers, by launching their generic drugs in the absence of other generic competitors, may have the advantage of being able to enter into long-term supply contracts with pharmacies retailing their products.[271]

Some observers, however, have questioned whether awarding 180 days of marketing exclusivity for first filers is necessary to encourage generic drug competition, particularly if the brand name drug has a large market.[272] Under these circumstances, they argue, the "threat of competition" provides an incentive to first applicants to enter the market as soon as possible, including possibly at risk, before subsequent applicants obtain approval of their ANDAs.[273] If exclusivity were the primary incentive for early generic drug entry, one might expect to find fewer subsequent paragraph IV challenges (because subsequent ANDA applicants are not awarded 180-day exclusivity). In fact, as the FTC has noted, the reduction in incentive for subsequent filers appears to be "small."[274] ANDA applicants have often filed paragraph IV challenges even when they have no or only a small chance of obtaining exclusivity. For instance, between 1991 and 1998, there were no awards of 180-day exclusivity to first filers; yet, the number and rate of paragraph IV filings "increased significantly" during that time.[275] And, as FDA noted in 2004 when denying a Mylan citizen petition relating to authorized generics, "[i]f 180-day exclusivity were the sole incentive for ANDA submission, FDA would presumably not see, as we do, second, third, and fourth ANDAs filed by generic companies that are aware that they are not the first to file an ANDA application including a paragraph IV certification and, therefore, cannot gain 180-day exclusivity."[276] These findings suggest that 180-day exclusivity, at least with respect to certain products, is not the primary incentive for seeking early generic entry into the market.

The authors' examination of drug products for which at least one first ANDA applicant filed an application containing a paragraph IV certification over the last

[266] FDA, *Generic Competition and Drug Prices*, *available at* http://www.fda.gov/cder/ogd/generic_competition.htm.

[267] *Id.*

[268] *Id.*

[269] *Id.*

[270] Tony Pugh, *Generics Will Benefit as 75 Drugs Lose Their Patent Protections*, KNIGHT RIDDER WASH. BUREAU, (Apr. 30, 2006).

[271] Kevin A. Hassett, & Robert J. Shapiro, *The Impact of Authorized Generic Pharmaceuticals on the Introduction of Other Generic Pharmaceuticals* 6 (Apr. 2007) (citation omitted), *available at* http://www.authorizedgenerics.com/downloads/ImpactofAuthorizedGenericPharmaceuticals.pdf.

[272] *See, e.g.*, Jeremiah Helm, Comment, *The Patent End Game: Evaluating Generic Entry into a Blockbuster Pharmaceutical Market in the Absence of FDA Incentives*, 14 MICH. TELECOMM. TECH. L. REV. 175, 191 (2007) (arguing that "generic firms will compete for entry without a 180-day exclusivity bounty as long as the market for the branded drug is large").

[273] *Id.* at 195.

[274] *See* Comment of the Staff of the FTC Bureau of Competition and of Policy Planning, FDA Docket No. 85N-0241 (Nov. 4, 1999), at n.27, *available at* http://www.ftc.gov/be/v990016.shtm#N_27.

[275] Ernst R. Berndt, et al., *Do Authorized Generic Drugs Deter Paragraph IV Certifications? Recent Evidence* 2 (Apr. 2007) (working paper) (citation omitted).

[276] FDA, Response to Teva and Mylan Citizen Petitions, Docket Nos. 2004P-0075 & 2004P-0261 (July 2, 2004), at 13.

four years indicates that the prospect of obtaining a period of 180-day exclusivity remains, at least for some generic manufacturers, a strong incentive.[277] While the number of drugs with a first filing held steady in 2005 and 2006, at 56 and 55 respectively, that number increased dramatically in 2007 to 84. In 2008, it declined to 70, but still represented a significant increase from 2005 and 2006. It is unclear to the authors whether this represents a meaningful change in ANDA filing rates or simply tracks changes in NDA approval rates (i.e., four years earlier), but it seems that ANDA applicants in the last two years have not been deterred by the fact that they may have to share their exclusivity periods with other first filers or even an authorized generic. In addition, these first filers were not deterred by the possibility of forfeiture under the new provisions. While these numbers suggest that 180-day exclusivity is an important factor generic manufacturers consider when deciding when to file their ANDAs, it is too early to draw any conclusions about the long-term effects of the changes included in the MMA and the emergence of authorized generics on these applicants' incentive to obtain generic exclusivity.

B. *Possible Topics for Legislation*

1. *Authorized Generics*

As explained in the authors' 2007 article, FDA and the courts have concluded that the FDCA does not preclude the holder of an approved NDA from marketing, or permitting the marketing of, an unbranded version of its product—a so-called authorized generic—during the exclusivity period or at any other time.[278] Notwithstanding the clear legality of this practice under the FDCA, questions regarding the effect of authorized generics on competition, particularly during the 180-day exclusivity period, have been raised.

Some claim that unbranded competition authorized by the innovator could discourage generic drug manufacturers from bringing paragraph IV challenges and marketing new generic products.[279] They contend that the 180-day exclusivity provision was intended to provide an incentive to generic drug manufacturers to challenge patents.[280] According to these opponents, authorized generic drugs reduce this incentive because they force generic manufacturers awarded 180-day exclusivity to share the period of exclusivity, thereby reducing profits and hindering the ability of these companies to recoup their litigation expenses.[281] Authorized generic products may, however, benefit consumers by promoting competition and reducing drug prices.[282] And arguably Congress indicated its support for price competition during the exclusivity term when it expressly recognized in the MMA that multiple

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[277] *See* FDA, *Paragraph IV Patent Certifications*, *available at* http://www.fda.gov/cder/ogd/ppiv.htm (as of Mar. 16, 2009).

[278] FDA, Response to Teva and Mylan Citizen Petitions, Docket Nos. 2004P-0075 and 2004P-0261 (July 2, 2004); Mylan v. FDA, 454 F.3d 270, 271 (4th Cir. 2006) (concluding that FDA lacks the power to prohibit the marketing of authorized generics during the 180-day exclusivity period); Teva Pharm. Indus. v. Crawford, 410 F.3d 51, 55 (D.C. Cir. 2005) (noting that the statute "clearly does not prohibit the holder of an approved NDA from marketing, during the 180-day exclusivity period, its own 'brand-generic' version of its drug").

[279] Congressional Research Service Report for Congress, Authorized Generic Pharmaceuticals: Effects on Innovation (Aug. 8, 2006) (CRS Report), at 1.

[280] *Id.* at 9.

[281] *See id.*

[282] *Id.* at 1.

first applicants could be awarded 180-day exclusivity.[283] While a number of studies on the effect of authorized generics on competition have been conducted, no consensus has been reached.[284]

Some members of Congress oppose the practice. Legislation to prohibit the marketing of authorized generics during the period of 180-day exclusivity was first introduced in the House of Representatives and Senate during the 109th Congress[285] and reintroduced in the 110th Congress.[286] None of these bills passed out of committee before the end of either Congress. Legislation has been reintroduced in the House of Representatives and Senate in the current Congress.[287] The House bill was referred to the House Committee on Energy and Commerce on January 15, 2009, and the Senate bill was referred to the Senate Committee on Health, Education, Labor, and Pensions on February 26, 2009.

As noted in the authors' prior article, Congress has also considered other measures relating to authorized generics. For instance, it included a provision in the Deficit Reduction Act of 2005 requiring that, after January 1, 2007, average manufacturer price and best price include all drugs marketed under a single NDA.[288] In addition, in 2005, Senators Grassley, Leahy and Rockefeller and Representative Waxman requested that the FTC conduct a study on the competitive effects of authorized generic drugs.[289] In April 2006, the Commission published a notice announcing its plans to examine the "likely short-term competitive effects of authorized generic drug entry" and "likely long-term impact of entry by authorized generic drugs on competition by generic manufacturers."[290] As part of this study, the FTC has requested detailed information from brand name, authorized generic, and generic drug companies. Although the Commission initially stated that the results of the study would be issued in 2007,[291] no results had been announced prior to publication of this article. One recent report noted that the FTC is currently in the process of analyzing the information it has collected but stated that the Commission has not publicly indicated the new timeframe for issuing its report.[292]

To facilitate this FTC study,[293] Congress included a provision in the FDAAA requiring FDA to publish on its website a list of all authorized generic drugs in-

[283] *See id.* at 14; *see also* section II. A. 2. b.

[284] *See, e.g.*, Ernst R. Berndt, et al., *Authorized Generic Drugs, Price Competition, and Consumers' Welfare*, HEALTH AFFAIRS (May-June 2007); Ernst R. Berndt, et al., *Do Authorized Generic Drugs Deter Paragraph IV Certifications? Recent Evidence* (Apr. 17, 2007) (working paper); Kevin A. Hassett, & Robert J. Shapiro, *The Impact of Authorized Generic Pharmaceuticals on the Introduction of Other Generic Pharmaceuticals* (Apr. 2007), *available at* http://www.sonecon.com/docs/studies/050207_authorizedgenerics.pdf; Aidan Hollis, & Bryan Liang, *An Assessment of the Effect of Authorized Generics on Consumer Prices* (July 2006); David Reiffen, & Michael R. Ward, *"Branded Generics" as a Strategy to Limit Cannibalization of Pharmaceutical Markets* (May 2005), *available at* http://ftc.gov/be/healthcare/wp/12_Reiffen_BrandedGenericsAsAStrategy.pdf; Bryan A. Liang, *The Anti-Competitive Nature of Brand Name Firm Introduction of Generics Before Patent Expiration*, 41 ANTITRUST BULLETIN 599 (Fall 1996).

[285] H.R. 5993, 109th Cong. (2006); S. 3695, 109th Cong. (2006).

[286] H.R. 806, 110th Cong. (2007); S. 438, 110th Cong. (2007).

[287] H.R. 573, 111th Cong. (2009); S. 501, 111th Cong. (2009).

[288] Deficit Reduction Act of 2005, Pub. L. No. 109-171, § 6003.

[289] 71 Fed. Reg. 16,779, 16,780 (Apr. 4, 2006).

[290] *Id.*; *see also* 72 Fed. Reg. 25,304, 25,305-25,306 (May 4, 2007).

[291] Press Release, FTC, FTC Proposes Study of Competitive Impacts of Authorized Generic Drugs (Mar. 29, 2006), *available at* http://www.ftc.gov/opa/2006/03/authgenerics.shtm.

[292] Cathy Dombrowski, *Authorized Generics Debate Heats up on Hill, But May Need FTC Study to Boil*, PINK SHEET, v. 71, no. 7 (Feb. 16, 2009).

[293] M. Nielsen Hobbs, *Authorized Generics: FTC Study May Get Jumpstart; PhRMA Paper Finds No Harm*, PINK SHEET v. 69, no. 18 (Apr. 30, 2007) (quoting Senator Brown, the author of the provision in the Senate, as stating that "[t]his amendment will help the FTC complete its work in a timely fashion").

cluded in annual reports submitted by NDA holders since 1999.[294] FDA must update this list quarterly.[295] In response to this mandate, FDA posted a list of authorized generics on its website.[296] On September 29, 2008, the agency announced that it intended to amend its regulations to require that NDA holders include information about authorized generic drugs in their annual reports.[297] Because FDA expected this amendment to be noncontroversial, it published the rule as a direct final rule, which would take effect on February 11, 2009. In accordance with FDA's guidance on direct final rule procedures,[298] the agency simultaneously published a proposed rule pursuant to the normal rulemaking procedures.[299] On February 10, 2009, FDA announced that it was withdrawing the direct final rule because the agency had received significant adverse comments and that it would develop a final rule pursuant to the notice-and-comment procedures.[300] It is not clear whether and how the agency intends to update the list on its website in light of the withdrawal of the direct final rule. One report, however, observed that it is unlikely the withdrawal of the direct final rule will affect the FTC's study given that the Commission has already assembled its own list of authorized generics based on the information it requested with respect to the study.[301]

2. *Settlement of Patent Litigation*

As noted above, if a first applicant enters into an agreement with another ANDA applicant, the NDA holder, or a patent holder, and the FTC or a court finds that the agreement violates the antitrust laws, the first applicant forfeits its eligibility for 180-day exclusivity.[302] Thus, the standards applied by courts to determine whether a settlement agreement violates the antitrust laws are relevant to 180-day exclusivity. A practice that has drawn criticism from some quarters and could eventually lead to the passage of legislation relates to the terms of settlement when innovators and generic applicants resolve patent litigation initiated in response to the filing of an ANDA containing a paragraph IV certification and the innovator provides something of value to the generic applicant.

The FTC has taken the position that these settlements "restrict competition at the expense of consumers, whose access to lower-priced generic drugs is delayed, sometimes for many years."[303] Based on its opposition to these settlements, the

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[294] *See* 21 U.S.C. § 355(t).

[295] 21 U.S.C. § 355(t)(1)(A)(ii).

[296] FDA, FDA Listing of Authorized Generics, *available at* http://www.fda.gov/cder/ogd/AG_Listing.htm.

[297] 73 Fed. Reg. 56,487 (Sept. 29, 2008).

[298] FDA, Guidance for FDA and Industry, Direct Final Rule Procedures (Nov. 21, 1997), *available at* http://www.fda.gov/opacom/morechoices/industry/guidance.htm.

[299] 73 Fed. Reg. 56,529 (Sept. 29, 2008).

[300] 74 Fed. Reg. 6,541 (Feb. 10, 2009). Comments from two pharmaceutical companies raised, in general, concerns about the potentially overbroad scope of the rule, the limitations on electronic submission of the information requested, and the fact that the rule does not prioritize currently distributed authorized generics. Letter from GSK to Division of Dockets Management, FDA (Dec. 11, 2008) (Docket No. FDA-2008-N-0341); Letter from AstraZeneca to Division of Dockets Management, FDA (Dec. 9, 2008) (Docket No. FDA-2008-N-0341).

[301] Cathy Dombrowski, *Authorized Generics Debate Heats up on Hill, But May Need FTC Study to Boil*, PINK SHEET, v. 71, no. 7 (Feb. 16, 2009).

[302] 21 U.S.C. § 355(j)(5)(D)(i)(V).

[303] *Hearing on H.R. 1902, Protecting Consumer Access to Generic Drugs Act of 2007, Before the Subcomm. on Commerce, Trade, and Consumer Protection of the House Comm. on Energy and Commerce*, 110th Cong. 1 (2007) (statement of the FTC).

Commission began to investigate and challenge these types of settlements in the late 1990s.[304] To facilitate its review of these settlements, Congress included a provision in the MMA requiring that all settlements reached in patent cases resulting from paragraph IV certifications be filed with the FTC and Department of Justice for review,[305] and it enacted the agreement forfeiture provision discussed in section III. A. 6. Notwithstanding the FTC's opposition to payments made by innovators to generic applicants in resolution of patent litigation and one appellate court decision in favor of the FTC's position,[306] two appellate court decisions in 2005, one from the Eleventh Circuit[307] and the other from the Second Circuit,[308] upheld such agreements. The Supreme Court declined to review either case.[309] In addition, the Court of Appeals for the Federal Circuit recently upheld such a settlement agreement.[310] A petition for a writ of certiorari for this latest case was pending at the time this article was written. In general, these appellate courts concluded that because a patent gives the owner a right to exclude competition, payments made to allegedly infringing applicants in exchange for a promise not to market are lawful as long as they do not exclude competition beyond the zone of exclusion of the patent at issue.[311]

In response to the 2005 decisions, legislation was introduced in Congress during the 109th and 110th Congresses that would have addressed agreements in settlements of patent infringement litigation involving payments from innovators.[312] In essence, these bills would have set out *per se* rules making certain kinds of "reverse payment" settlements, in which patent owners provide something of value to the generic applicants, into antitrust violations. Hearings were held on the issue during the 110th Congress, and representatives of both the innovator and generic drug industries opposed utilizing a *per se* rule, favoring instead a "rule of reason" analysis of the facts of the particular case to determine whether an agreement is anticompetitive.[313] Although the Senate bill was reported out of the Senate Judiciary Committee, it was not considered by the full Senate.[314] Similarly, a hearing was held by the Subcommittee on Commerce, Trade and Consumer Protection of the House Committee on Energy and Commerce on one of the House bills during the

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[304] *Id.* at 2, 14.

[305] *See* Pub. L. No. 108-173, § 1112 (2003).

[306] *See In re* Cardizem CD Antitrust Litig., 332 F.3d 896 (6th Cir. 2003), *cert. denied*, 543 U.S. 939 (2004).

[307] Schering-Plough Corp. v. FTC, 402 F.3d 1056 (11th Cir. 2005), *cert. denied*, 548 U.S. 919 (2006).

[308] *In re* Tamoxifen Citrate Antitrust Litig., 429 F.3d 370 (2d Cir. 2005), *amended*, 466 F.3d 187 (2d Cir. 2006), *cert. denied*, 127 S. Ct. 3001 (2007).

[309] In both cases, the Solicitor General filed a brief with the Supreme Court opposing the Court's review. Brief for the United States as Amici Curiae, Joblove v. Barr Labs., Inc., 2007 WL 1511527, No. 06-830 (2007); Brief for the United States as Amici Curiae, FTC v. Schering-Plough, Corp., No. 05-273, 2006 WL 1358441 (2006).

[310] *In re* Ciprofloxacin Hydrochloride Antitrust Litigation, 544 F.3d 1323 (Fed. Cir. 2008), *cert. petition filed*, No. 08-1194 (Mar. 23, 2009).

[311] *See, e.g., id.* at 1336 ("The essence of the inquiry is whether the agreements restrict competition beyond the exclusionary zone of the patent.")

[312] *See, e.g.*, S. 3582, 109th Cong. (2006); S. 316, 110th Cong. (2007); H.R. 1432, 110th Cong. (2007); H.R. 1902, 110th Cong. (2007).

[313] *Paying Off Generics to Prevent Competition with Brand Name Drugs: Hearing Before the Senate Comm. on the Judiciary*, 110th Cong. (2007) (testimony of Billy Tauzin, CEO, PhRMA, and Bruce Downey, Chairman and CEO, Barr Pharmaceuticals).

[314] All Congressional Actions for S. 316 (110th Cong.), *available at* http://www.thomas.gov/cgi-bin/thomas.

110th Congress.[315] The bill was then referred to the Subcommittee on Courts, the Internet, and Intellectual Property of the House Judiciary Committee. It, however, was never reported out of committee. Similar legislation has been introduced in the current Congress, and the Subcommittee on Commerce, Trade, and Consumer Protection of the House Committee on Energy and Commerce held a hearing on the House bill on March 31, 2009.[316]

While the FTC has expressed support for legislation prohibiting innovator payments to allegedly infringing generic applicants,[317] it has also continued to challenge settlements involving such payments. As discussed above in section III. A. 6. b., the Commission filed a complaint against Cephalon in the U.S. District Court for the District of Columbia in February 2008,[318] alleging that Cephalon engaged in "a course of anticompetitive conduct that is preventing competition to its branded drug Provigil."[319] According to the FTC, "[t]he conduct includes paying four firms to refrain from selling generic versions of Provigil until 2012."[320]

More recently, in January 2009, the FTC filed a lawsuit in the United States District Court for the Central District of California, challenging agreements by Watson Pharmaceuticals, Par Pharmaceuticals Companies and Paddock Laboratories "to delay until 2015 the sale of low-cost generic versions of AndroGel, a widely prescribed branded testosterone replacement drugs, in exchange for substantial payments from Solvay."[321] The FTC has indicated that, by bringing such challenges, it is trying to create a split in the circuit courts and increase chances of review of the issue by the Supreme Court.[322]

These challenges could have significant implications for the first filers, as well as the subsequent generic applicants. If, as noted in section III. A. 6. b., the FTC is successful in either of these actions at the appellate level, the forfeiture provision could be triggered, thus resulting in a loss of all or part of exclusivity for these first filer(s) if they have not already launched their products or, if they have, if 180 days have not already passed. Success in such challenges could also more broadly affect the opportunities for settling litigation and, thus, the costs of challenging and defending patents.

C. *Adaptation of the Model for Other Contexts*

As noted earlier in this article, 180-day exclusivity was designed as an incentive to challenge innovator patents. There is evidence that it has provided some degree

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[315] *Hearing on H.R. 1902, Protecting Consumer Access to Generic Drugs Act of 2007, Before the Subcomm. on Commerce, Trade, and Consumer Protection of the House Comm. on Energy and Commerce*, 110th Cong. (2007).

[316] S. 369, 111th Cong. (2009); H.R. 1706, 111th Cong. (2009).

[317] *See, e.g., Hearing on H.R. 1902, Protecting Consumer Access to Generic Drugs Act of 2007 Before the Subcomm. on Commerce, Trade, and Consumer Protection of the House Comm. on Energy and Commerce*, 110th Cong. 1-2 (2007) (statement of the FTC).

[318] FTC v. Cephalon, Inc., No. 08-cv-00244 (D.D.C. Feb. 13, 2008) (complaint). At Cephalon's request, this case has been transferred to the U.S. District Court for the Eastern District of Pennsylvania. *See* FTC v. Cephalon, Inc., No. 08-cv-02141 (E.D. Pa. May 8, 2008).

[319] Press Release, FTC, FTC Sues Cephalon, Inc. for Unlawfully Blocking Sale of Lower-Cost Generic Versions of Branded Drug Until 2012 (Feb. 13, 2008), *available at* http://www.ftc.gov/opa/2008/02/ceph.shtm.

[320] *Id.*

[321] FTC v. Watson Pharms., Inc., No. 09-cv-598, at 2 (C.D. Cal. Jan. 27, 2009) (complaint).

[322] *See Senators, FTC Seek to Ban "Reverse Payments" Between Brands, Generics*, FDA WEEK (Feb. 6, 2009).

of incentive, and many products are subject to paragraph IV certifications.[323] It is less clear how much of an incentive it is, and how many paragraph IV certifications would have been submitted in the absence of 180-day exclusivity. What is also not clear is the extent to which the incentive leads to too much litigation, and possibly even litigation spawned more for the opportunity to obtain the exclusivity than would be generated just due to the substance of the patent challenge.

A more recent question is whether this type of incentive is suitable in other contexts. The principal area in which an exclusivity incentive roughly analogous to 180-day exclusivity has been considered is the area of developing a regulatory approval pathway for follow-on biologics, where there could be legislation that could lead to establishing a process for challenging biologics patents.[324] The FTC held a roundtable on issues relating to the topic of follow-on biologics and specifically encouraged consideration whether a patent-challenge based incentive was warranted and whether some other type of incentive was warranted.[325] There were numerous comments critical of implementing an incentive like 180-day exclusivity that could be an incentive for increased litigation. Some favored establishing an incentive that would encourage certain types of applications. The FTC has yet to release the results of the roundtable. It is noteworthy that no bill on follow-on biologics introduced during the 110th Congress contained a patent-based incentive. Two bills recently introduced in the 111th Congress, however, do have incentives built around filing for and obtaining approval of certain kinds of applications (relating to the potential for products to be considered "interchangeable").[326] It remains to be seen whether Congress will in the end favor this kind of incentive.

[323] *See* FDA, Paragraph IV Patent Certifications, *available at* http://www.fda.gov/cder/ogd/ppiv.htm (as of Mar. 16, 2009).

[324] *See* S. 1695, 110th Cong. (2007); H.R. 5629, 110th Cong. (2008).

[325] *See* 73 Fed. Reg. 51479 (Sept. 3, 2008).

[326] H.R. 1548, 111th Cong. (2009); H.R. 1427, 111th Cong. (2009).